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TUMOURS OF THE NASOPHARYNX

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(*Continued from previous issue*)

Malignant Tumours

According to most of the authorities malignant tumours of the nasopharynx are far more common than the benign tumours. Thomson and Negus (*loc. cit.*) are of opinion that innocent growths are so uncommon that every new growth in this region should be looked upon with suspicion. Stout (*loc. cit.*) finds that malignant tumours are thrice as frequent as benign tumours. There were 22 cases of malignant tumours in this series, which is just a little more than the number of benign tumours. This disparity in this series as compared with others is due to the incidence of far larger number of naso-pharyngeal fibromata.

Etiology—Of the 22 cases 18 were males and 4 females. This preponderance in the male sex is in agreement with the general experience of American as well as that of Chinese workers.

Age—The table below shows the age incidence in each decade in this series.

Age period	*No. of cases*	*Per cent*
1 to 10	2	9
11 to 20	0	0
21 to 30	6	27
31 to 40	11	50
41 to 50	3	14

The youngest in the series (*vide* fig. 5) was a female child of four. Probably she had a sarcomatous tumour. There was another case of a male child of 10 years of age, a victim to fibrosarcoma.

It is well known that sarcoma may occur at any age. But what is noteworthy is that carcinoma also is seen in the naso-pharynx at an earlier age than in any other part of the upper respiratory tract. The youngest in the series of Klienfeld (1936) was 14 years of age. Stimson's patient as quoted by Wishart (1941), suffering from an epidermoid carcinoma, was a boy of ten years of age. More remarkable is Figi's case, as quoted by Wishart (*loc. cit.*), where squamous-called carcinoma with bilateral glands occurred in a boy of 11 years. He was treated with radium when he became well. He reported after ten years for treatment of an area of actinodermatitis on either side of his neck. Digby and his associates (*loc. cit.*) also noted the early age of onset. They also remarked that the disease occurs not very frequently in young adults and even in older children. The youngest patient in this series is a male of 22 years of age, a subject of lymphoepithelioma.

The environmental and racial factors and their relative role in the predisposition to this disease in the Chinese in such large numbers have already been discussed. Apparently, the etiology of these tumours is more obscure than of cancer elsewhere. The nasopharynx is not subject to the more common forms of chronic irritation.

Pathology—Histological confirmation of the diagnosis after a biopsy could be obtained only in 9 out of 22 cases and the results have already been noted in the classification of the tumours.

In the remaining 13 cases, biopsy was not considered desirable or was not consented to by the patient, or the piece taken and sent was not representative and failed to help the diagnosis. But from the rapidity of growth, presence of glandular metastasis and the invasive propensities already exhibited there was clinically no doubt as to their malignancy and many of them appeared to come under the category of carcinomata. Martin and Blady as cited by Jeune (1941) observe "Because nasopharyngeal cancer originates most frequently in the region of the nasopharyngeal tonsil, it is natural that highly anaplastic epidermoid carcinomata and lymphosarcomata should make up a large proportion of these cases." Highly differentiated squamous-celled carcinomas and spindle-celled sarcomas made up a smaller number. Amongst the

epitheliomata the controversy over the inclusion of lympho-epithelioma as a clinical entity is not yet come to a close. Stewart leans back to the old designation of lymphosarcoma. Tetrud is of opinion that no distinction should be drawn between transition-celled carcinoma and lymphoepithelioma. Boyd thinks that lymphoepithelioma is a subgroup of transition-celled carcinoma. New expressed the opinion that all tumours arising from epithelial structures should be called squamous-celled carcinoma grade IV. Munro-Black (1938) points out that sarcomata occur in life during the growing period and lympho-epithelioma in the involuting or involuted lymphoepithelial regions, a feature common to epithelioma in general, though he also says that the entity of lymphoepithelioma is not yet accepted.

Stout (*loc. cit.*) concludes this controversy by saying that very probably lymphoepithelioma is simply a histological variant of the undifferentiated epithelioma. But whatever its origin, it has morphological features which are distinctive enough to enable us to segregate it from both the undifferentiated epithelioma on the one hand and from the reticulum-celled lymphosarcoma on the other, to both of which it bears some resemblance.

Whatever be the ultimate decision of the pathologist as to the precise classification of these tumours, it is somewhat reassuring that all the malignant tumours of the pharynx are reported to be very radio-sensitive and their histopathology is not of such great importance from the point of view of their treatment.

Sarcoma often attains some size, presents irregular or lobulated, greyish or pinkish white surface and it may be soft to the touch. It displaces rather than infiltrates.

Epithelioma is medium-sized, of a deeper colour, not painful, usually ulcerates, fungates and bleeds.

Lymphoepithelioma, pink and firm begins and spreads deeply and subepithelially. It appears on the surface and ulcerates only later. Metastasis in the regional lymph glands is often the first sign and is practically a constant feature. But it is not unique to this tumour.

Cancer of the nasopharynx occurs most often in the posterior wall, in the region of the pharyngeal tonsil and on the lateral walls. It may originate lower on the posterior wall but practically never from the anterior wall or the floor. In this series amongst the tumours reported upon histologically, it will be noticed that there is an adenolymphoma and a rhabdomyoma. Both the tumours appear to be rare and histologically should probably have been classed under benign growths but from their clinical characteristics I have preferred to group them under malignant tumours. A short resume of the two cases is as follows;—

Case 1—A Hindu male, 14 years, admitted on 24-6-38 with a complaint of nasal obstruction and bleeding. *Anterior rhinoscopy*—A hard mass filling up the inferior meatus of the right side. *Posterior rhinoscopy*—A roundish swelling about the size of a small lemon seen on the nasopharynx a little to the right of the middle line. It was examined under general anæsthesia and a biopsy done. The growth appeared to have arisen from the posterior wall of the nasopharynx, felt hard and of cartilaginous consistency. It was extending into the right nasal cavity displacing the septum. There was no ulceration. *X-ray*—Lateral view shows a hazy shadow in the region corresponding to the intravertebral disc between first and second cervical vertebræ and loss of continuity of the line of the anterior surface of the first cervical vertebra. *Histopathological report*—The tumour is lined by stratified epithelium on the surface and shows a structure with dilated lymphatics, with hyperplastic lymphatic tissue in between. In this area are embedded tubular structures lined by stratified epithelium. The structure is suggestive of adenolymphoma.

The response to radium treatment was not quite satisfactory.

Case 2—A Hindu male, 62 years, admitted with a complaint of difficulty in swallowing, change in voice and noises in the left ear.

There was a fleshy growth (*vide* Fig. 6) pushing the pillars of the left fauces and the soft palate downwards and forwards and the uvula was pushed to the right. The fringe of the left anterior pillar was tightly stretched over the growth. There was no pain or tenderness. It bleeds easily. *Origin*—nasopharynx. *X-ray of the nasal accessory sinuses* showed nothing abnormal. *Transillumination* revealed the left antrum less translucent. *Histopathological report* on the biopsy specimen: "The tumour has the structure of a cellular fibroma but also contains a large number of striated muscle fibres. It is covered on the surface by stratified squamous epithelium. Rhabdomyoma."

Tumours consisting of the striated muscle are very rare. According to Boyd they do not occur in voluntary muscle but they are usually found in the kidney, testicle and vagina. Radium treatment did not seem to be of any benefit.

Schall and Cordray as reported by Wishart (1942) report a rhabdomyosarcoma of the posterior septum in a boy of 6. They say these mixed tumours are highly malignant and metastasise by blood stream. These tumours are not radio-sensitive. The treatment should be surgical.

Symptoms and signs—There may be no symptoms in the early stages. When they become manifest they may be divided up into three groups:

1. Local symptoms are due to local lesion and referable to the nose and nasopharynx. These are nasal obstruction, discharge, postnasal discomfort, pain or sore throat, sensation of a lump in the throat and epistaxis. As the growth extends and involves the neighbouring structures (*vide* Figs. 7 and 8), ear symptoms such as a feeling of deafness, tinnitus, stuffiness, proptosis and trismus are also complained of.

2. Neurological symptoms. The growth (Figs. 9, 9A, 10, 11 and 11A) extends to the sphenoid bone and the floor of the middle cranial fossa on either side of the sella turcica. The tip of the petrous bone may be destroyed. The disease may extend into the orbit through the sphenoidal fissure and posteriorly between the dura and the base of the skull producing pressure on the cranial nerves one after another. Excepting the VIII and VII which are to some extent protected by their position on the back of the petrous bone and by their immediate entry into the internal auditory meatus, all the other cranial nerves are apt to

FIG. 5.—Hindu, F. C., 5 years
Malignant growth in the nasopharynx, probably a sarcoma. Youngest in this series.

FIG. 6.—Hindu, M., 62 years
Rhabdomyoma. Radium treatment was of no avail.

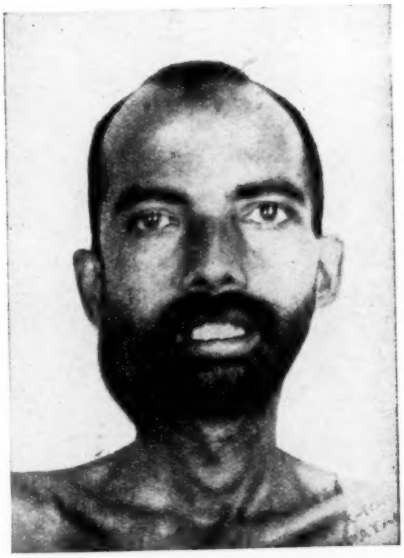

FIG. 7.—Hindu, M., 30 years
Malignant growth nasopharynx. Started with noises and pain in the right ear.

FIG. 8.—Hindu, M., 30 years
Lymphosarcoma (?) nasopharynx. Started with noises in the right ear. Responded well to deep x-ray therapy.

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FIG. 8A.—Same patient as in FIG. 8 After deep x-ray treatment. Shows ptosis. Later on developed 'jugular foramen syndrome' and bilateral external rectus (ocular) paralysis.

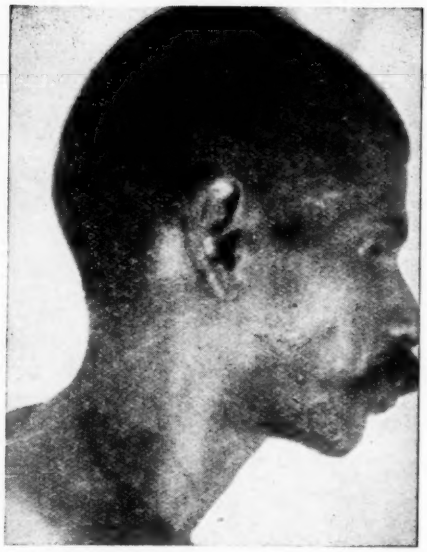

FIG. 9.—Hindu, M., 40 years Lymphoepithelioma nasopharynx. Started with intense pain in the right temporal region and ringing noises in the ear. Cervical glands slightly enlarged.

FIG. 9A.—Same patient as in FIG. 9 Shows greater enlargement of cervical glands and exophthalmos, four months later.

FIG. 10.—Hindu, M., 50 years Malignant growth nasopharynx. His complaint first started with intense radiating neuralgic pain right side of the head. Later on developed right external rectus paralysis. This is illustrative of the syndrome of the point of the petrous.

be involved. The V and VI and its divisions are the most frequently affected.

3. Enlargement of the Lymphatic glands. The group of glands behind the angle of the jaw and high up in the neck are involved at first. They rapidly increase in size and the other groups of glands in the neck are also enlarged. Enlargement of the glands in the neck may be the first symptom and ultimately they are enlarged in all cases which remain untreated. Pressure of the enlarged deep cervical glands on the neighbouring cranial nerves gives rise in turn to facial paralysis, jugular foramen syndrome, paralysis of the tongue and Horner's syndrome either singly or in combination. Finally, generalised matastasis occurs in the lungs, spine or the abdomen. The general condition steadily and rapidly deteriorates with severe anæmia and cachexia (*vide* Figs. 12 & 13).

Various authorities have given various percentages of the first appearance and predominance of the groups of symptoms above stated. Of the patients in this series a large majority presented themselves so late in the course of the disease that it was not possible to elicit always accurately the first symptom and the duration of the disease. Classified on the basis of the predominant groups of symptoms, it was found that 7 cases or 32 per cent fall in the first group, 4 cases or 18 per cent in the second group and 11 cases or 50 per cent in the third group. Intolerable and incessant headache was the only symptom complained of by one patient, which was already of six months' duration when he presented himself and it was only after repeated examination that the growth in the nasopharynx was spotted out.

In another patient the first symptom was intense neuralgia of the cheek and forehead and he later developed VI nerve paralysis (homolateral). This syndrome has been called by the French "The syndrome of the point of the petrous".

There was no complaint except glandular enlargement in two patients and a small growth in the nasopharynx was detected by posterior rhinoscopy.

On examination the nasopharynx discloses variable findings. The tumour may look very much like a mass of adenoids but deeply coloured. It may be smooth, velvety or ulcerated. A large mass filling the nasopharynx pushing the soft palate down is more common with sarcomata.

Extension under the mucosa may give rise to a flat and firm swelling. It may be very extensive and may not ulcerate; This has already been pointed out as a characteristic of lympho-epithelioma.

The glands in the neck are frequently enlarged bilaterally but one side is affected earlier than the other. The glands underneath the sternomastoid and the posterior triangle of the neck are also involved. They are hard like rubber and matted together.

In addition evidence of the involvement of one or more of the cranial nerves is present and in fact it may be the first symptom for which advice is sought for by the patient.

Diagnosis—There is often inordinate delay in arriving at a diagnosis as the disease has few or no symptoms at all in the early stages, the examination is difficult and requires some skill which most physicians neglect to acquire and practise. The nasopharyngoscope should supplement the information obtained by the mirror examination. Palpation with the finger of the nasopharynx does not often help as much as one would expect. Lastly, direct inspection of the nasopharynx with elevation of the soft palate by means of a rubber catheter may have to be resorted to. Yankeur's tubular speculum may be helpful but I have not used it. There are two points in diagnosis, first the presence of a tumour, second the nature of the tumour. A clinical picture referable to unilateral implication of cranial nerves issuing from the middle or posterior cranial fossæ should make one search for retro or sub-maxillary cervical glands. The detection of enlarged glands should be followed by repeated and thorough examination of the nasopharynx.

The "syndrome of the point of petrous bone," present in 80 per cent of the cases in the neurological group may be confused in the initial stages with paroxysmal trigeminal neuralgia or tic douloureux. In this latter affection there are no objective sensory changes, the pain is sharper and associated with the trigger zones, stimulation of which produces pain. There is no involvement of the motor root or of any other cranial nerves.

Petrositis and sphenoidal sinusitis have also to be excluded.

There is no tendency for the enlarged glands to break down as in tubercular affection. Finally a biopsy of the lesion, if any, in the nasopharynx, or of one of the enlarged cervical glands should settle the diagnosis. Munro-Black (*loc. cit.*) warns that biopsy should be done just before irradiation for fear of enhancing the possibility of metastasis or immediately afterwards as the tumour may have disappeared, if waited too long after irradiation. Biopsy is preferably done by the diathermy knife.

Treatment—In all highly malignant cases which special predeliction for early metastasis, surgery holds out little or no hope. Malignant growths of the nasopharynx offer few exceptions to this general rule. In addition, owing to inaccessibility, extreme vascularity, and rapid infiltration into the cranium, surgery and diathermy are generally considered unsuitable. Nor surgery has any pace in the treatment of cervical metastasis, which are often bilateral and widespread and recurrence is almost immediate.

The tumours, as a rule, are extremely radiosensitive and the location will tolerate heavy doses of irradiation. Irradiation, therefore, is the method of choice. Interstitial and surface application of radium is yeilding place gradually to deep x-ray therapy either alone or in combination. X-ray is simpler and considered quite adequate.

The futility of surgical treatment was brought home to me quite a long time ago. In a case of lymphosarcoma, it was noticed that no sooner the glands on one side were removed by block dissection, than glands on the other side of the neck began to grow with alarming rapidity. The glands on the second side were dissected a fortnight later and both internal jugular veins had to be sacrificed. I gave up all hope of the patient surviving the second operation but nothing untoward happened. As there was some interval between the ligature of one internal jugular vein and the other, collateral circulation was amply established. Secondary deposits were detectable in the lungs by x-rays in this patient. He finally died of shock and hæmorrhage after the operation for expiration of the primary tumour.

Very soon after this bitter experience, we got our radium in 1931 and ever since no attempt was made at surgical treat-

ment except in a female patient with a lymphoepithelioma where the glands were removed on one side again with the same result as in the patient with lymphosarcoma described above. A young man suffering from intense agonising headache was admitted in our hospital last year. After most thorough and repeated examinations a small growth was detected in the roof of the nasopharynx (Fig. 11). A biopsy of a gland was done and it was declared to be a lymphoepithelioma. Fortunately, he took our advice and went to Madras for deep x-ray therapy. He returned in three months to my great surprise and delight with complete relief from his symptoms. I have not heard from him since and I cannot say anything about his further progress.

A large majority of the patients were admitted so late in the course of the disease that with the small quantity of radium at our command nothing more than a partial relief from symptoms could be achieved. This was, of course, temporary and it could not have lasted longer than a few months. A follow-up study of these cases was not successful.

There has been, of course, with improved technique of treatment and possibly earlier diagnosis, a steady improvement in the results obtained, which have already been published by several authorities. Treatment by irradiation has distinctly improved the outlook.

Kasabach (1941) reports that 14 out of 42 cases treated by x-ray (33 per cent) are alive and well at the time of reporting and 7 out of them (16 per cent) are clinically free from disease for over five years.

Coutard, as cited by Martin (1939), reported 10 per cent of 89 cases free from symptoms at the end of 5 years. The results are more striking in the lymphoepithelioma and lymphosarcoma group in his series. Lymphosarcomas, as a rule, require relatively less irradiation and may be eradicated by a smaller total dose. Lymphoepithelioma group has shown a far more favourable prognosis and longer survival period than any other group.

The prognosis was grave in patients with bilateral cervical metastasis and also in most cases with bone destruction.

The only hope at present lies in early diagnosis of the lesion, while it is still limited to the nasopharynx and administration of vigorous irradiation to all the known paths of extension.

Summary and Conclusion

We cannot rest content with the belief that the tumours of the nasopharynx are not common, in view of the increasing evidence to the contrary.

The etiology of malignant disease of the nasopharynx is more obscure than its incidence elsewhere in the upper respiratory tract. The extraordinary susceptibility of the Chinese to this disease is probably racial and may have nothing to do with their environment. The report of Kulley (*loc. cit.*) of the large number of cysts discovered by him during the short space of six years brings out prominently the necessity of routine examination of the nasopharynx.

Nasopharyngeal fibroma has been considered in all its aspects and stress has been laid upon the avoidance, if possible, of biopsy for diagnosis and of surgery in treatment. The etiology, pathology and the insidious character of the symptoms of malignant disease of the nasopharynx have been discussed. The importance of repeated and thorough examination of the nasopharynx, whenever indicated, was noticed. The precautions to be observed in making a biopsy have been mentioned. It is hoped that with the fast improving technique in radiotherapy, this distressful problem may soon be solved.

References

Digby, K. H. and others—*Brit. J. Surg.*, **28**:517-37, 1941.

Figi, F. A.—*J.A.M.A.*, **115**:665-72, 1940.

Hauser, I. J. and Brownell, D. H.—*Ibid*, **111**:27 & 2467, 1938.

Jeune, F. E. and Bayon, P. J.—*Laryngoscope*, **51**:1003 & 1004, 1941.

Kasabach, H. H.—*Laryngoscope*, **51**:459-63, 1941.

Kleinfeld, L.—*Ibid*, **46**:1415, 1936.

Kulley, B. M.—*J. Laryng. & Otol.*, **50**:317-28, 1935.

Martin, C. I.—*Am. J. Rœntgeonol*, **41**:377-89, 1939.

Munro-Black, J. I.—*J. Laryng. & Otol.*, **53**:225-43, 1938.

Stout, A. P.—*Laryngoscope*, **51**:446-50, 1941.

Thomson, St. Clair and Negus, V. E.—Disease of the Nose and Throat. Fourth Edition, 1937. Published by Cassell & Co., Ltd., London, p. 345.

Wishart, D. E. S.—*Laryngoscope*, **51**:785 & 770, 1941. *Idem—Ibid*, **52**:666 & 667-68, 1942.

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FIG. 11.—Hindu, M., 22 years
Lymphoepithelioma nasopharynx. Youngest in the series. Intense headache was the first symptom. Relieved with deep x-ray therapy.

FIG. 11A.—Same patient as in FIG. 11
Lateral view showing slight enlargement of the glands under the sternomastoid which were absent when first seen five months previously and when his only complaint was headache and trismus.

FIG. 12.—Hindu, F., 26 years
Malignant growth nasopharynx. Started with tinnitus. Growth seen in the right nostril also. Cervical glands markedly enlarged.

FIG. 13.—Hindu, F., 40 years
Malignant growth nasopharynx. Started with enlargement of lymph nodules left side. Both sides show their extensive involvement.

HÆMATOLOGICAL STUDIES IN THE NEWBORN

WITH SPECIAL REFERENCE TO BLOOD CHANGES DURING THE FIRST WEEK

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Although much has been written on the blood condition of the infants and nurslings, yet the blood picture of the newborn has not been fully investigated. The results of the various observers in this field have been controversial. The present study was undertaken in order to observe the normal blood picture of the newborn in the Queen Mary's Hospital, Lucknow. The blood of the newborn was examined for the total red blood corpuscles, hæmoglobin percentage and total and differential white blood corpuscle counts. All the twenty five cases included in the series were normally delivered, and no anæsthetic was used. The umbilical cord was clamped after the cessation of pulsation. The blood was examined within fifteen minutes of the birth and the examination was repeated on the first, third, sixth and ninth days after birth. The blood was taken by a deep stab on the heel. It has been very difficult to keep in touch with the cases under study and hence every attempt to investigate further was frustrated.

The accompanying tables (Tables I and II) show the detailed hæmatological picture as obtained in our investigation: Table I gives the figures for total red blood corpuscles, hæmoglobin percentage (100 per cent being equivalent to 15 gm.) and the size of the red blood corpuscles. Table II shows the total and differential values of white blood corpuscles.

Analysis

Let us now analyse these findings one by one.

Red Blood Corpuscles—The blood is thick and difficult to spread on the slide. General blood picture shows immature nucleated red blood cells, anisocytosis, poikilocytosis, and polychromatophilia. Reticulocyte count was not done. The results are tabulated below:

R.B.C. Count in Million per c.mm.

After birth	*Minimum*	*Maximum*	*Average*	*S.D.*
Within 15 min. ..	4·18	7·77	5·65	± 0·985
1st day ..	3·7	6·44	5·19	± 0·877
3rd „ ..	3·78	6·6	5·005	± 0·852
6th „ ..	3·44	5·89	4·45	± 0·729
9th „ ..	3·45	5·72	4·61	± 0·802

The total red blood cells count thus ranges between 4·18 to 7·7 million per c.mm. of blood. The blood count is highest at birth and gradually falls down till it takes the picture of the nursling.

The newborn possesses a number of red blood corpuscles considerably in excess than that found normally in adults. In the first day or two of the life the average number is nearer 6 million than 5 million and in exceptional cases it may be as high as 7 million. Megaloblast and mesoblast are present (Thursfield, 1934). The number of red blood cells in newly born infants was approximately 5,500,000 per c.mm. and the figure declined to 3,900,000 per c.mm. on between second and third months (Faxen, 1937). The blood of the newborn contains a large number of nucleated red blood cells. They do not tend to collect in rouleaux and show very little or no central depression. The number of red blood cells ranges from 5,000,000 to 7,500,000 per c.mm. Person and Wyllie (1935) give figures as high as 6,500,000 per c.mm. Hutchinson (1904) estimates upto 6,000,000 per c.mm. The summary of further data from the literature is given below:—

	R.B.C. per c.mm. of blood
Hayem (quoted by Ewing, 1903) ..	5,368,000
Sorenson ditto ..	5,665,000
Helot ditto ..	5,531,000
Otto ditto ..	6,165,000
Faxen (1937)	5,500,000

Mean Diameter of the Red Blood Corpuscles: Following is the table showing the average mean diameter of the red blood cells. It will be seen that an average red blood cell of the newborn is bigger than matured ones.

No. of subjects	*Time of examination*	*Diameter in microns*
25	Just after birth ..	.. 7·5
	1st day after birth ..	.. 7·53
	3rd „ „ „ ..	.. 7·5
	6th „ „ „ ..	.. 7·56
	9th „ „ „ ..	.. 7·4

Haemoglobin Percentage: The hæmoglobin content of the blood of the newborn taken from the heel was estimated by Hellige Hæmoglobinometer. The average results of hæmoglobin percentage (100 per cent hæmoglobin is equivalent to 15 gm.) are as follows:—

After birth	*P.C.*	*S.D.*
Within 15 min.	149·4	± 18·87
1st day	142·1	± 20·34
3rd day	139·72	± 12·02
6th day	132	± 14·02
9th day	128·24	± 22·91

The hæmoglobin content of the blood is higher at birth and begins to fall gradually. It ranges from 116 to 183·6 per cent at birth.

To determine the relationship between the blood of the umbilical cord and the blood taken from the heel, comparative hæmatological study was undertaken in eight cases. The results are presented in a tabular form.

TABLE I—SHOWING THE TOTAL RED BLOOD CORPUSCLES, HAEMOGLOBIN PERCENTAGE AND THE SIZE OF R. B. C. OF INFANTS.

Serial No.	*Just after birth*			*1st day after birth*			*3rd day after birth*			*6th day after birth*			*9th day after birth*		
	Total R.B.C. in million	Hb %	Size of R.B.C. in microns	Total R.B.C. in million	Hb %	Size of R.B.C. in microns	Total R.B.C. in million	Hb %	Size of R.B.C. in microns	Total R.B.C. in million	Hb %	Size of R.B.C. in microns	Total R.B.C. in million	Hb %	Size of R.B.C. in microns
1.	5·15	144·3	7·7	5·12	134·2	7·6	4·56	134	7·5	4·44	129	7·4	4·19	120	7·4
2.	4·64	130·5	7·8	4·19	120·3	7·8	3·92	120·8	7·8	3·82	118	7·5	3·55	106	7·5
3.	6·45	164·2	7·2	5·77	151·8	7·4	5·61	141	7·4	5·1	140	7·6	5·08	136	7·5
4.	5·07	135·7	7·3	4·96	134	7·2	4·74	133·8	7·2	4·3	126	7·4	4·1	120	7·4
5.	5·22	145	7·6	5·14	135	7·6	4·89	134	7·4	4·5	130	7·6	4·46	120	7·6
6.	4·18	116	7·6	3·56	112	7·6	3·28	114	7·5	3·44	92	7·3	3·45	77·2	7·3
7.	4·99	135	7·2	4·89	127·6	7·6	4·65	127·7	7·6	4·12	124·7	7·4	3·9	118·2	7·4
8.	6·04	159·5	7·8	5·6	150	7·6	5·6	140	7·6	5·10	139·1	7·4	5·02	132·2	7·4
9.	6·93	175·7	7·3	6·04	174	7·2	6·04	154·8	7·3	5·85	150	7·2	5·7	165·5	7·3
10.	5·51	150	7·6	5·28	139·2	7·6	5·01	137	7·6	4·7	134	7·6	4·9	127	7·6
11.	5·6	150·2	7·5	5·45	140	7·5	5·04	137·7	7·5	4·8	134·5	7·4	4·9	127	7·3
12.	4·94	134·5	7·8	4·75	127·5	7·8	4·36	127	7·8	4·08	124·7	7·8	3·81	116	7·6
13.	6·8	169·2	7·4	5·88	165·5	7·5	5·84	143·5	7·6	5·38	145	7·4	5·58	150	7·4
14.	4·45	126	7·6	3·7	116	7·5	3·78	120·7	7·8	3·57	117	7·5	3·55	104·5	7·3
15.	7·77	183·6	7·0	6·44	185·6	7·1	6·6	156·5	7·1	5·89	154	7·1	5·72	178·5	7·1
16.	5·65	151	7·8	5·49	145	7·8	5·4	139·2	7·8	4·81	135	7·8	4·96	130	7·4
17.	4·67	131·4	7·3	4·23	121·7	7·2	4·15	124	7·2	3·86	119	7·5	3·6	114	7·4
18.	6·68	163·8	7·5	5·88	162·4	7·4	5·73	143	7·6	5·24	145	7·6	5·41	148	7·3
19.	4·2	124·8	7·8	3·7	114	7·5	3·78	119·5	7·4	3·49	116	7·2	3·45	100	7·2
20.	6·88	174	7·1	6·38	170	7·2	5·89	153	7·2	5·5	150	7·2	5·62	156·4	7·2
21.	4·9	133	7·4	4·31	124	7·7	4·15	126·7	7·5	3·92	121	7·5	3·72	115	7·5
22.	5·7	159·5	7·6	5·49	145	7·4	5·6	139·7	7·4	5·01	137	7·4	4·96	130	7·4
23.	6·64	168·3	7·5	5·84	153	7·4	5·64	141·9	7·4	5·19	145	7·4	5·1	139	7·4
24.	6·84	170	7·9	6·19	169	7·8	5·84	149·7	7·8	5·49	146	7·8	5·6	151·1	7·6
25.	5·37	145	7·2	5·2	135·7	7·5	4·97	134	7·5	4·7	130	7·5	4·8	124·4	7·5

TABLE II—SHOWING THE TOTAL AND DIFFERENTIAL WHITE BLOOD CORPUSCLE COUNTS IN INFANTS

Serial no	*Just after birth*				*1st day after birth*				*3rd day after birth*				*6th day after birth*				*9th day after birth*		
	Total Count	Differential Count			Total Count	Differential Count			Total Count	Differential Count			Total Count	Differential Count			Total Count	Differential Count	
		Poly	Lympho	Eosino		Poly	Lympho	Mono		Poly	Lympho	Eosino		Poly	Lympho	Mono		Poly	Lympho
1	18,800	66	34	...	13,000	68	32	...	10,560	82	14	4	11,600	62	38	...	10,000	60	40
2	21,800	84	16	...	20,200	78	22	...	13,000	69	31	...	18,600	70	30	...	17,600	68	32
3	14,240	76	24	...	14,700	74	24	2	13,760	73	27	...	10,800	12	88	...	9,840	...	...
4	24,000	70	30	...	19,200	70	30	...	13,000	65	35	...	11,000	63	37	...	19,000	80	20
5	14,380	75	25	...	12,700	74	26	...	12,200	80	20	...	10,020	66	34	...	8,720	70	30
6	16,000	72	28	...	14,800	70	30	...	12,200	72	28	...	10,800	76	24	...	9,800	70	30
7	9,360	68	32	...	24,000	54	46	...	11,200	72	28	...	8,720	74	26	...	11,280	74	26
8	11,700	90	9	1	10,240	92	8	...	8,000	94	6	...	7,400	65	35	...	7,900	66	34
9	15,500	68	32	...	28,800	76	24	...	19,600	71	29	...	12,600	40	60	...	16,500	54	46
10	14,080	75	25	...	22,020	95	5	...	12,800	84	16	...	10,800	60	37	3	9,240	62	38
11	16,640	77	23	...	20,720	69	31	...	15,000	56	44	...	11,400	70	30	...	19,720	84	16
12	14,600	80	20	...	14,720	54	46	...	14,000	80	20	...	13,180	64	36	...	16,800	72	28
13	20,200	62	38	...	30,400	76	24	...	10,400	65	35	...	17,000	81	18	1	13,380	65	35
14	23,000	68	32	...	12,800	92	8	...	12,000	77	23	...	18,000	70	30	...	12,600	75	25
15	10,800	53	47	...	21,600	71	29	...	8,030	72	28	...	11,840	68	32	...	9,800	55	45
16	24,160	70	30	...	19,000	69	31	...	12,500	69	30	1	10,720	68	32	...	9,200	72	28
17	15,208	85	15	...	22,440	78	22	...	15,000	70	30	...	15,400	58	42	...	18,000	60	40
18	15,840	92	8	...	22,600	78	22	...	19,760	65	35	...	16,800	59	40	1	15,300	65	35
19	11,000	75	25	...	8,800	72	28	...	9,200	70	30	...	8,000	68	32	...	7,240	60	40
20	16,030	62	38	...	15,000	66	34	...	12,220	62	35	3	10,800	58	42	...	9,800	64	36
21	13,720	65	35	...	20,160	62	38	...	15,000	80	20	...	11,700	60	40	...	18,720	72	28
22	12,820	70	30	...	10,230	69	31	...	8,000	69	31	...	7,400	50	50	...	9,000	60	40
23	18,220	56	43	1	14,720	62	38	...	8,960	62	38	...	11,220	56	44	...	12,240	70	30
24	22,410	74	26	...	21,550	80	20	...	11,720	86	14	...	15,560	62	38	...	18,200	78	22
25	11,400	70	30	...	10,000	81	19	...	8,000	80	20	...	13,220	50	50	...	11,600	54	46

COMPARATIVE STUDY OF THE BLOOD FROM UMBILICAL CORD AND BLOOD TAKEN FROM THE HEEL OF THE NEWBORN

	Blood from the umbilical cord		*Blood from the heel taken within 15 minutes of birth.*	
	R.B.C. in million per c.mm.	*Hb. p.c.*	*R.B.C. in million per c.mm.*	*Hb. p.c.*
1.	3·82	116	5·05	170
2.	3·54	135·3	6·45	145
3.	3·57	104·3	4·18	116
4.	3·47	106·5	5·99	133
5.	3·4	116	5·93	169·2
6.	3·27	129	5·51	134·5
7.	3·99	100	5·56	135
8.	3·22	125	7·77	159·5

WHITE BLOOD CORPUSCLES: The average white blood corpuscle count on different days is given below:

TOTAL W.B.C. COUNT

Just after birth	16,036 per c.mm.
1st day „ „	16,898 „ „
3rd day „ „	12,517 „ „
6th day „ „	12,183 „ „
9th day „ „	12,086 „ „

DIFFERENTIAL W.B.C. COUNT

	Poly. per cent	*Lympho. per cent*	*Eosino. per cent*	*Mono. per cent*
Just after birth ..	72·1	26·8	0·1	—
1st day „ „ ..	73·2	26·7	—	0·1
3rd day „ „ ..	73	26·7	0·3	—
6th day „ „ ..	61·2	38·6	—	0·2
9th day „ „ ..	67·1	32·9	—	—

The blood picture shows general leucocytosis. The white blood cell count is higher at birth and gradually falls upto the sixth day, when it is 12,183 per c.mm. and then it again rises to 12,806 on the ninth day. The differential white blood cell count shows relative preponderance of polymorphs which gradually decrease with a consecutive rise in the number of lymphocytes.

A comparative analysis of the findings of other workers in the same field may be of some interest. The following table gives such values:

DIFFERENTIAL W.B.C. COUNT OF THE NEWBORN

Name of Investigator		*Neutro. per cent*	*Lympho. per cent*	*Mono. per cent*	*Eosino. per cent*
CARSTANJEN (1900)	1st day	37·45	16·05	8·6	1·9
	3rd „	66·18	18·84	11·25	3·73
	6th „	41·81	38·11	18·27	4·81
	9th „	36·11	41·86	19·32	2·7
	12th „	36·69	16·67	1·54	48·6
GUNDOBIN (1893)	Just after birth	63	25	12	
	24 hrs. „ „	68	24	8	
	48 hrs. „ „	70	21	9	
	5 days „ „	60	32	8	

DISCUSSION

It is difficult to explain the polycythæmia of the newborn infant. Ewing (*loc. cit.*) found that polycythæmia bears a close relation to the degree of cyanosis exhibited at birth. Postnatal dehydration has been advanced as a possible explanation, but it looks highly improbable that the change would occur within from a few minutes to less than half an hour. The oxygen-content of the fœtal blood in sheep is found to be higher than that of the maternal blood (Barcroft *et al*, 1938). A higher red blood cell count and hæmoglobin percentage might be an attempt on the part of Nature to provide the fœtus an atmosphere of much higher oxygen saturation.

The concentration of the blood might be principally referable to the relative state of stasis which is then established in the peripheral capillaries. It might be helped by the slowing of the heart rate which occurs at clamping. Bauer (1937) experimenting in fœtal sheep found that the fall in the rate of heart beat which occurred at birth may be due to slowing of the whole heart rather than due to vagal stimulation. The newborn infant's hæmopoietic system is very sensitive to the changes in the environment. Polycythæmia due to splenic contraction during emotional excitement has been observed in the cat (Izquierdo and Cannon, 1928). The smooth muscles of the fœtus are relatively inactive. The smooth muscles of the lamb's spleen begin to contract at birth. So, it is thought there might be similar contraction of the spleen, throwing more blood in the general circulation.

The average red blood cell count at birth in this series is 5,650,000 per cubic millimetre. This figure is nearly the same as found by other observers. However, I would like to emphasise the importance of noting the exact time of clamping the umbilical cord. Different investigators may get varying results if the umbilical cord is clamped immediately or after cessation of pulsation or after the placenta is out of the uterus. Pulsation indicated that the vessels of the placenta are not yet occluded. It has been noted that cessation of pulsation does not necessarily indicate that the placental capillaries have emptied themselves of the blood. The blood from the placenta can be driven out as a result of the compression of the placenta by the contracting uterus, aided by the constriction of the vessels of the placenta and the thoracic aspiration, even when the pulsation of the umbilical cord has ceased. Frischkarn and Rucker (1939) found that the red blood cell count was higher (5,780,000 per c.mm.) in those infants whose umbilical cord was clamped late as compared to those in which it was done early (5,200,000 per c.mm.). Other observers have noted that the initial loss of weight in the first few days after birth is usually less in cases where the ligation of the umbilical cord is slightly delayed. The blood from the umbilical cord is lower in red blood cell content and hæmoglobin percentage as compared with the blood taken from the infant's heel as is shown by the comparative analysis of blood from both these sources in eight cases.

Duke and Stofer (1922) also found that the number of red blood cells in the capillary blood was higher than that in the venous blood in pernicious anæmia. They suggested that the macrocytes occluded the capillaries and led to concentration of the corpuscles there. In the case of the newborn also the same may happen.

The hæmoglobin in the newborn fluctuates from 90 to 115 per cent and gradually falls to 70 to 80 per cent in from 3 to 4 weeks after birth. According to Hutchinson (*loc. cit.*), hæmoglobin content is as high as 110 per cent at birth. Carstanjen (1900) estimates it as 100-120 per cent at birth. The mean value of hæmoglobin is 22·7 gm. per 100 c.c. of blood during first week of life (Faxen, *loc. cit.*). The average figure of the cases investigated by me is 149·41 per cent or 22·41 gm. per 100 c.c. blood. My figures are higher than those of the other workers mentioned above.

The differential count of white blood cells further gives some points of difference between the present and other workers. It will be seen that the number of monocytes, as determined by the author, is much below the number given by Carstanjen (*loc. cit.*) and Gundobin (*loc. cit.*).

Gundobin gives a higher percentage of polymorphs than Carstanjen. Thursfield (*loc. cit.*) describes that the white corpuscles also undergo a slow diminution. There is a marked fall in number in first few days. The total number of polymorphonuclear cells which is from 18,000 to 25,000 per c.mm. at birth quickly reaches the normal level of 5,000 to 6,000; the total number of lymphocytes at birth is from 3,000 to 5,000 per c.mm. and rises during the first few weeks of life from 7,000 to 9,000 per c.mm. Thus the ratio of polymorphs to lymphocytes at birth is 6 or 5 to 1. At birth high leucocytic counts always occur. There are different views on this point; the figures are usually between 15,000 to 30,000 per c.mm. of blood, average being 20,000 leucocytes per c.mm. After a slight rise in the beginning, the number decreases reaching its lowest point on the following days (on from third or fourth to sixth day) to about 7,000-10,000; it then rises (second elevation) finally changing into the constant blood picture of nurslings by the tenth to fourteenth day.

The blood picture at birth is markedly neutrophilic.

Summary

1. Hæmatological findings in 25 newborn babies at different periods have been presented.
2. The literature has been reviewed critically in view of the present findings.
3. Average hæmoglobin, red blood cell and white blood cell counts did not always follow the values found by other observers. The mean average hæmoglobin was higher than other workers (149·41 per cent). The value of red cell count was nearly the same as that found by the other workers (5,650,000 per c.m.). White blood counts, specially the differential count showed much variation—number of monocytes being much below the number given by other workers.
4. Importance of the time of clamping the umbilical vein on the variation of the red cell count has been stressed. To show the variation, a comparative study of the blood from both the umbilical vein and the heel was done in eight cases.

References

Barcroft *et al.*—*J. Physiol*, **93**:23, 1938.
Bauer, D. J.—Proceedings of the Physiological Society, 8th May, 1937.
Carstanjen, M.—*Jahrb. f. Kinderh*, **52**:215, 1900.
Duke, W. N. and Stofer, D. D.—*Arch. Int. Med.*, **30**:94, 1922.
Ewing, J.—Clinical Pathology of Blood. Published by Henry Kimpton, London, 1903.
Faxen, N.—*Acta Pediat.*, **19**:1, 1937.
Frischkorn and Rucker—*Am. J. Obst. & Gynec.*, **38**:592, 1939.
Gundobin, N.—*Jahrb. f. Kinderh*, **35**:187, 1893.
Hutchinson, R.—*Lancet*, **1**:253, 1904.
Izquiredo, J. J. and Cannon, W. B.—*Am. J. Physiol*, **84**:545, 1928.
Pearson and Wyllie—Recent Advances in Diseases of Children. Published by J. & A. Churchill, London, 1935.
Thursfield, Garrod and Paterson—Diseases of Children. Published by Arnold. London, 1934.

WANTED DOCTORS

Copy of letter No. 01119, dated January, 21, 1944, from the Secretary, Servants of India Society, Poona-4 (India) to the Secretary, Indian Medical Association, Calcutta:

"I send herewith copy of a cable received to-day from the India Club, Port of Spain, Trinidad. I shall be obliged if you will kindly bring the contents of the cable to the notice of the members of your body, with a view to ascertaining if any of them would be prepared to take advantage of the offer.

As I am expected to cable my reply early next month, I shall be glad if I could have your reply by the end of this month."

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"Vacancies exist twenty Physicians Surgeons with qualifications Registered with General Medical Council, Great Britain. Could you select suitable candidates and inform us if they would be prepared to out here on five year contract? Commencing Salary Fifty Pounds per Month. Advisable select candidates with Highest Professional Qualifications."

Intending candidates are advised to communicate direct with the Secretary, Servant of India Society, Poona-4 (India).

P. B. Mukerji,
Hony. General Secretary,
Indian Medical Association

27-1-43

THE VALUE OF SULPHATHIAZOLE IN CUTANEOUS COCCAL MANIFESTATIONS

(IMPETIGO, FURUNCULOSIS AND FOLLICULITIS)

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Introduction

One of the commonest skin affections is coccal infection of varying nature. The two common pathogenic cocci to produce skin affections are the streptococcus and staphylococcus but to associate each with a particular lesion or to expect to find one brand of cocci in a particular variety of skin affection is incorrect. It has been customary to streptococci with impetigo contagiosa, ecthyma, bullous impetigo and pemphigus neonatorum, while the staphylococci were identified with boils, folliculitis with sycosis and Bockhart's impetigo. The two often go together and to call one the primary causative agent and the other a super-added or secondary factor is incorrect.

The three common coccal affections of the skin are (1) impetigo of different types and intensities, (2) furunculosis and (3) folliculitis (general) or sycosis (barber's region). Often streptococci are dominant in impetigo and the staphylococci in the two latter. More often the two are present together and it is idle to attempt to discriminate the so-called primary from the secondary. Such an attempt is justified from the therapeutic standpoint, if we have specific chemotherapeutic agents for streptococcus as distinguished from staphylococcus or perhaps to be more scientific and precise, streptococcus viridans from streptococcus militans. Was not sulphanilamide first believed to be effective only against streptococcus beta-hæmolyticus, and today has it not been proved to act on cocci, bacilli, gram positive, gram negative, capsulated, non-capsulated, aerobic and anaerobic? Nay, it has over-stepped the coccal-bacterial realm and promises to be useful in protozoal and viral affections.

Hence without attempting to discriminate the causal bacteriological factor. we studied the effect of Sulphathiazole* in some cutaneous coccal manifestations.

Chemistry and Action

Cibazol claims to belong to the sulphathiazole group. Its empirical formula is $C_9H_9N_3O_2S_2$, *i.e.*, 2-sulfanilylaminothiazole. It is derived from the basic sulphanilamide $C_6H_4NH_2SO_2NH_2$ by the substitution of the amido group. By the substitution of the amino group, we get compounds like Proseptasine, Soluseptasine, Rubiazol, etc.

The amido substitution (sulphonamide) derivatives have been found to be useful in pneumococcal, gonococcal, meningococcal and staphylococcal infections, while the amino (NH_2) substitution derivatives and the basic sulphanilamide have been found useful in streptococcal infections. But clinical observers have so far found one group of derivatives useful (varying in extent) in both classes of infections though sulphanilamide has little effect in pneumonia. The disinfectant action is greater at 40°C than at 37°C and suggests that the drug depresses bacterial metabolism. The different bacteria probably are alike basically with regards to their metabolism and any of the sulphanilamide derivatives should do well, barring, of course, variation in degree, to an appreciable extent. Acute conditions where it is surmised that the organisms are in a state of rapid multiplication, respond well to any of this group of drugs, which again bears out with the assumption that their metabolism is interfered with and rapid growth inhibited. A concentration of about 10 mgm. per 100 c.c. is desirable in acute conditions. Acute pneumonia, for example, needs a bigger dose than gonorrhœa and still less is required in the treatment of coccal infections of the skin. It is not yet established definitely whether a high concentration of the drug at a time or a moderate but uniform and prolonged concentration, is essential in the treatment with this drug. Like salicylates in rheumatic fever, maximum possible dose is needed in pneumonia for as long a period as 36 to 48 hours though not quite on the verge of toxic dose as with salicylates.

Sulphathiazole in Cutaneous Infections

The recognised treatment of impetigo and allied infections is by a mild antiseptic. Unna is of opinion that after the executive phase, impetigo treated with a paste of 1 per cent hydrarg ammoniate-zinc oxide effected a certain cure. Indeed he claimed this therapeutic test for its diagnosis. A starch poultice is often recommended at the commencement of the treatment to remove the crusts or scabs and to enable the medicament to come into contact with the area. A few applications of this paste generally effect a cure. In our experience, though this treatment was the main-stay, it was not so effective as claimed. Possibly, the preliminary poultice application which was left to the patient was not carried out properly.

We had also tried extensively the application of 2 per cent solution of gentian violet on exudative and crusty impetigenous lesions without the preliminary poultice application. For all other cases of folliculitis, sycosis, furunculosis (multiple small boils) we applied the gentian violet paint freely and daily. The result were fairly satisfactory, in many cases, though speedy and certain cures were rare. We had also tried intravenous administration of gentian violet in 0·5 per cent strength, 2-5 cc. to cases of folliculitis and sycosis with no encouraging results. (5 mgm. per kilo of gentian violet is suggested for intravenous therapy, but we did not dare to attempt this heroic dose).

Recently it was suggested that applications of liquor ferri perchlor fortis to impetigenous lesions did well. We have also been trying this in this clinic though as yet no definite view could be vouchsafed. In a few cases of extensive, intractable, coccal infections in children, sulphathiazole was tried as a last measure and the effect was dramatic.

* Our thanks are due to the manufacturers, Ciba (India), Limited, Bombay, for a liberal supply of their preparation. The samples primarily intended for being tested in gonorrhœa, were also tried in certain skin diseases with definite success in both.

A selected number of cases in the dermatological clinic were chosen for trial, particularly the extensive and acute form, where the curative effect could be unmistakably perceived. Mostly children with acute impetigo-exudative, purulent and scabbing over extensive areas on the face and extremities, were selected. Details of a few typical cases are given below.

We tried the effect also on multiple furunculosis with or without associated impetigo. Here again the result was quite satisfactory. In both these conditions it was noticed that children bore the drug in doses of one gram a day very well with no toxic manifestations of any kind. Their age ranged from 2 to 8.

We next tried the effect of Sulphathiazole in folliculitis and sycosis in adults. The dosage had to be restricted to 2-3 grams a day for three days. Though beneficial effects were noticed, they were not so definite as in the two previous conditions. Perhaps, investigations with increasing dosage for a longer period may reveal better results in folliculitis.

Case Reports

The following illustrative cases are cited:

Case 1—Krishna Veni, female child, aged 8. Extensive coccal infections of both hands and legs below the elbow and knee respectively. General condition bad, slight temperature, unable to walk with commencing œdema of feet. Both hands were clawed. 1 per cent hydrarg ammoniata-zinc paste for two days had no effect. General condition was worsening. Cibazol, half a tab (0·25 gram) was given four times a day with plenty of water for two days. The effect after two days was miraculous. The scabs and pustules had completely disappeared, the areas started to heal up and the child was able to walk, definitely cheerful and with all evidence of improved general condition.

Case 2—Savitri, female child, aged 6. Extensive coccal infections of both legs, with coalesced infected areas oozing serous discharge. General condition of the child was poor. Gentian violet application for three days showed no appreciable effect. One tablet (0·5 gram) of Cibazol twice a day was administered as there was no evidence of kidney damage, as in Case 1. The response was very satisfactory. The parents, unfortunately, continued to apply some oil to the area otherwise the lesions would have been dry. A further half a gram twice daily for another day without the application of oil revealed the drying and healing process unmistakably.

Case 3—Krishna Lal, male child, aged 9. Multiple boils on the face and neck with extensive coccal infection of the face and scalp. The boils ranged in size from a pea to a big marble, some of them fluctuating. The two lachrymal sacs looked infected and the two "boils' were pointing from near the inner canthus of the two eyes. The child had fever and the general condition was poor. The eyelids could be opened only with difficulty. The conjunctivæ were not involved. Lymphatic glands in the neck were standing out prominently and some were soft. Two boils on the neck were incised and the pus let out. Gentian violet application was not of much effect. The child was put on Cibazol, 0·5 gram twice daily for two days. He was advised to be brought after an interval of a day for incising two more of the boils. When the child was brought as advised, there was a change beyond recognition. The eyelids had opened, the two boils that were to be incised that day were missing and the general condition had improved a lot. Two more tablets of half a gram each were given for two more days and the child had apparently completely recovered.

Case 4—Medical student, aged 21, with extensive furunculosis of face attended with fever. The size of the boils ranged from 1½ to 1 inch in diameter, red and inflamed. Some showed pus points. Two tablets of Cibazol (0·5 gram a tab) were given twice a day for two days. On the third day all the boils had disappeared except one. He was again put on two tablets twice a day and the last and the biggest of the crop also showed signs of disappearing, the inflammation subsided and the fever came down to normal.

Case 5—Simhachallam, male, aged 25. Extensive folliculitis of the outer aspect of the leg below the knee on both sides with sycosis of the beard region. The beard region was covered with crusty scabs and on close observation, many of the hair follicles were found to be filled with pus. The legs were glossy with purulent hair follicles and some scattered superficial ulcers. The conditions had been there for over two years according to the history. Hydrarg ammoniata (B.P.), citrine ointment, gentian violet application and auto-hæmotherapy had all been tried in succession with no appreciable effect. The patient was then put on two tablets (0·5 gram each) of Cibazol twice a day for three days. The effect was not so dramatic as in furunculosis and impetigo but there was satisfactory evidence of the healing process having started. The purulent follicles had almost disappeared and the process of scabbing had started. After about a week he was advised to shave the beard region (till then he was clipping the beard) to observe if the region was healing. The shave did no harm as it scraped off the dry scabbed crusts. Hypo-pigmented surfaces over the healed region were seen. The legs were also fairly healthy though the glistening surface of the skin was there, revealing thereby the non-subsidence of the inflammation. For about a week subsequently there was no reappearance of folliculitis or sycosis. He was advised to continue the gentian violet paint as a prophylaxis as also for psychic reasons, as most cases of folliculitis become neurotic.

Several more cases belonging to these three groups revealed that Cibazol treatment has very good effect in acute impetigo and furunculosis though in folliculitis and sycosis it is not quite so good.

Discussion

The action of sulphanilamides on streptococcus beta-hæmolyticus and other bacteria has been shown to be, by the prevention of utilisation of a substance essential for their growth and metabolism. This essential factor has also been found to be para-aminobenzoic acid. Various other substances of known chemical composition are also needed for their growth. It

is for the future chemical bacteriologist or the bacteriological chemist to find the most essential of these growth factors and if the growth factor varies from cocci to cocci or cocci to bacteria. But so far, sulphanilamide and its derivatives, inhibit the growth of many and varied organisms, which seem to indicate that most pathogenic organisms need para-aminobenzoic acid. At least this is one of the essential growth factors or is it that the drug has inhibiting influence on other growth factors, their nature and specificity not yet disclosed? Field and his collaborators (1942) observed that there being a close and simple relationship between para-aminobenzoic acid—the growth factor and sulphanilamide—the growth inhibitor, it can be predicted that a compound having this relationship to another growth factor will inhibit growth by preventing utilisation (pantothenic acid seems to be another essential growth factor for many organisms.) Hence the idea of sulphanilamide therapy seems to be to sweep the system of one or more of these essential growth factors and 'starve' the organisms to death. Acute conditions like pneumonia and to some extent gonorrhœa seem to demand more of the drug to remove or neutralise more of these growth factors while sub-acute or chronic affections like skin infections, need less. There is certainly the factor of the degree of susceptibility of the different species of organisms. From the low dosage needed in skin infections, one may justifiably conclude that either there is not active or rapid multiplication of the organism or that they are more easily susceptible to the drug. Beinhauer (1941) used sulphathiazole in treating more than 100 cases of skin infections like furunculosis, impetigo, lupus, erythematosis coccal complications of fungal diseases, acne vulgaris, pemphigus, etc. The dose consisted of half a gram four times a day for adults. The authors had found that it had a dramatic effect in pustular acne. In our series the acute forms of impetigo and furunculosis respond almost 'specifically'. The clearing process in impetigo or coccal dermatitis was rapid and dramatic, while the absorption or disappearance of pus from moderate-sized furuncles was quick. The chronic folliculitis or sycosis reacted favourably though less dramatically than the two previous conditions. But a word of caution is necessary. Though the pustules dry up rapidly, they tend to reappear in smaller numbers if the treatment is stopped after three or four days. It is essential, therefore, that the treatment should be continued for a week or ten days after the apparent disappearance of the lesions, if recurrences are to be avoided.

Conclusions

1. Sulphathiazole was found to be very effective in impetigo and furunculosis in a short series of cases.
2. Children below the age of eight responded very well.
3. The dosage was small, *i.e.*, a gram a day for two days for children from 3-8 years and two grams twice a day for adults.
4. In folliculitis and sycosis, the effect though not as dramatic as in the other two, was yet satisfactory. Perhaps bigger dosage or prolonged treatment may yield better results.

References

Beinhauer, *et al—Arch. Dermat. & Syph.*, **43**:621, 1941.
Field and Associates—*Brit. M. J.*, **2**:223, 1942.

DETERMINATION OF HÆMOGLOBIN VALUES

PLEA FOR A CONVERSION CHART

NITYANAND TYAGI, subedar, I.A.M.C.

In present day hæmatology, many new terms have been introduced which are apt to confuse the practitioner. Matters are made worse by the failure of the hæmatologists to agree among themselves as to the exact meaning and scope of some of the terms they employ. The impression might be gained from some of the recent writings that an accurate diagnosis of anæmia can only be arrived at after examination of sternal marrow smears and that a study of the peripheral blood is not sufficient. Such an outlook is a source of bewilderment to the general practitioner and it would be as well to state quite categorically that the simple procedures open to him will enable him to arrive at an accurate diagnosis in the great majority of cases. The study of the peripheral blood smear and the evaluation of the colour index still remain the corner stones of the diagnosis of the varying types of anæmia. My purpose is to discuss the colour index, to point out certain fallacies in its estimation and to suggest a method whereby it may be arrived at more accurately.

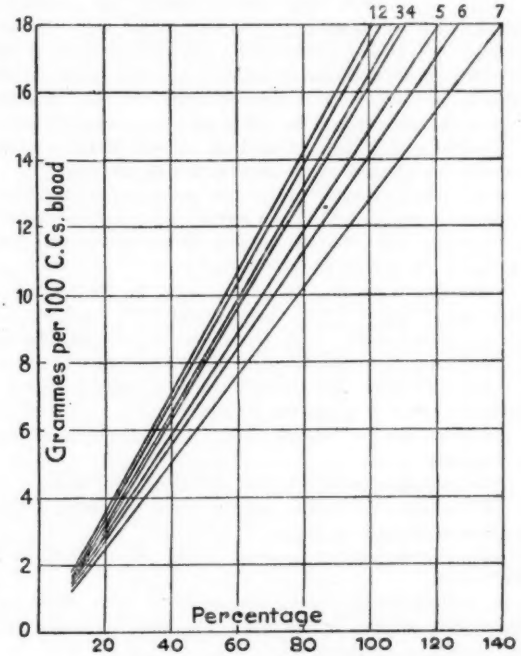
The C.I. is derived from the fraction p.c. Hb./p.c. R.B.C. Enumeration of the red cells is a simple procedure: a multiplication of the figure, in million by 20 gives the percentage of the normal, since 5 million is the accepted normal, *e.g.*, R.B.C.s=1·5 million: percentage is therefore $1{\cdot}5\times20=30\%$. The difficulty, however, is in the estimation of the Hb. There are numerous methods employed for the purpose but those available to the general practitioner are based on colour matching. It must be remembered that this particular method is the least accurate of all but, if care is exercised in technique, the interpretation becomes standardised and uniform.

There are many hæmoglobinometers in the market and whichever is used the clinical worker must adhere minutely to the details laid down by the manufacturer, since each instrument is tested and standardised. In employing a colour matching method, there is always on error (+ or − 5%) due to personal factors and failure to follow the instructions will lead to gross aberrations. For example, the Sahli's hæmoglobinometer, if advised to be read after ten minutes, should be read in exactly that time: if this is exceeded, a deduction of 2% must be made in the reading.

The percentage obtained from the scale should not be taken as an abstract figure since such a percentage on one instrument is by no means the equivalent of the same percentage on another maker's apparatus. For example, 100% on Tallqvist scale is equivalent to 15·8 grammes of Hb. per 100 c.c. of blood, whereas 100% on the Sahli scale means only 13·8 grammes, while on Dare's scale it is as much as 16 grammes. Should, therefore, the percentage read from one or other scale be employed in the calculation of the colour index, it is obvious that greatly differing results will be obtained, varying with the particular instrument employed by the clinician. To give a concrete example, with a

red cell count of 2 million, it is possible on varying instruments to obtain percentages of Hb. of 35, 40 and 45 respectively. This would give colour indices of below unity, unity and above unity, respectively and three different observers would, therefore, regard the same case as hypochromic, orthochromic and hyperchromic. To obviate this difficulty it is necessary to establish the "true" hæmoglobin percentage, based on the accepted normal standard of 14·5 grammes per 100 c.c.'s of blood.

Unfortunately, none of the makers supplies a conversion chart, from which the particular percentage on the instrument can be read off as the "true" percentage on this basis, although some modern instruments such as the Sahli-Hallige, do give the equivalent grammes per cent alongside their percentage scale. I have attempted to remedy this defect by plotting a graph showing (a) grammes per cent and (b) the equivalent "true" hæmoglobin percentage, as compared with the readings of most



HAEMOGLOBIN CONVERSION GRAPH

1 denotes Sahli's (old model). 2 Newcomer's. 3 Dare's (new model). 4 Tallqvist's. 5 Haldane's, Sahli Hellige's and True percentage. 6 Sahli's (new) and Dare's (old model). 7 Sahli's (Hawksley made).

Direction for use—On the base (abscissa) note the per cent figure as obtained on the hæmoglobinometer in use. From that point go vertically up to meet the line representing the instrument used. From the point of intersection go parallel to base line and read:

(*i*) Hb "gms. per cent" on vertical line (ordinate)
(*ii*) Hb "true per cent" on line no. 5.

of the hæmoglobinometers in common use. The instruments with which I deal are as under:—

(*i*) Dare's new and old models. (*ii*) Sahli's new and old models. (*iii*) Hawksley-type Sahli. (*iv*) Sahli-Hellige. (*v*) Newcomer. (*vi*) Haldane. (*vii*) Tallqvist.

The last, *i.e.*, Tallqvist, is mentioned only to be condemned: its margin of error, both personal and actual, is so great that it is useless in the calculation of the colour index. This criticism, of course, does not detract from the value of this method of hæmoglobin estimation for rough clinical purpose.

The use of the 'Hæmoglobin Conversion Graph' which is annexed should help to standardise the colour index and remove the more common sources of error. The correlation of the colour index with a study of peripheral smear will, as I have said, enable the practitioner to arrive at an accurate diagnosis in the great majority of the anæmias with which he will have to deal.

In the absence of the 'Hæmoglobin Conversion Graph', "true" hæmoglobin reading may be derived from the instrumental readings by the employment of the factor noted against each instrument in the following table:—

Dare's new model	multiply by	1·103.
„ old „	„ „	0·952.
Sahli's old „	„ „	1·193.
„ new „	„ „	0·952.
„ (Hawksley made)	„ „	0·855.
„ Hellige's	„ „	1·000.
Newcomer's	„ „	1·167.
Talliqvist's	„ „	1·090.
Haldane's	„ „	1·000.

(*Continued from page 149*)

Unfortunately, no skiagram of the chest could be taken due to very low condition of the patient. Post-mortem examination was also not possible as relatives refused permission, otherwise much light could have been thrown on the pathology of the lesion, etiology, etc.

The following features of the case are interesting—

1. It is one of the rare conditions and the first authentic case recorded at the Patna Medical College Hospital.
2. No definite literature exists to show that pyopneumothorax can result from this cause.
3. Causation is vague.
4. The fetor of breath and the fetid sputa, so characteristic of this condition, were remarkably absent all through the disease.

ACKNOWLEDGMENT

My thanks are due to our Principal and Professor of Medicine, Dr. T. N. Banerjee, M.R.C.P., and our Superintendent, Dr. B. P. Varma, for kindly giving me permission to publish this case. I must also thank Prof. B. N. Prasad, F.R.S. (ED.), and Dr. S. K. Ghosh Dastidar, M.R.C.P., for constant encouragement and guidance without which it would not have been possible to publish this case.

EFFECT OF DIFFERENT CONVULSANTS ON THE BIOCHEMISTRY AND CYTOLOGY OF BLOOD

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Biochemical changes of blood like uræmia, hypoglycæmia, hypocalcæmia, conditions of acidosis and alkalosis and accumulation of metabolites (guanidine and methylguanidine) in the circulating blood have been well recognised factors in precipitating convulsions in human beings. Convulsions or fits are observed in all periods of life from infancy to old age and represent a clinical syndrome caused by many different etiological factors.

They may be a symptom of birth trauma, congenital cerebral defect, hypertrophy of the brain, mechanical or emotional trauma, spasmophilia, tetany, severe burns, meningitis, reflex irrition, gastrointestinal intoxication, intestinal parasites, diseases of the heart and kidneys and various other conditions like hysteria, epilepsy, etc. Animals when they have to raise the temperature of the body go into convulsions. Rigor in children is generally represented by convulsions. In many of the convulsive states where the causes are not definitely known changes in blood chemistry have been noted during postconvulsive stage, though no such changes have been recorded to exist in between the convulsions. Such changes always accompanied severe convulsions, no matter what the type of convulsions, although they may be missed in some milder forms. Changes in cytological constituents of the blood have been noted in rigor.

The object of this work is to determine what changes in blood chemistry like glucose, urea, calcium, chlorides, and pH are produced by different convulsants. Not only this, but the cytological aspect of the changes *i.e.* changes in erythrocyte count, leucocyte count and differential count has been studied.

Convulsant drugs can be divided into the following groups according to their site of action: (1) Cerebral convulsants, *e.g.*, camphor; (2) medullary convulsants, *e.g.*, picrotoxin, metrazol. (3) spinal convulsants, *e.g.*, strychnine; (4) peripheral convulsants, acting on motor nerve, *e.g.*, aconitine and acting directly on muscles, *e.g.*, veratrine.

It was proposed to try one drug of each convulsant group on a number of different animals *viz.*, dog, cat, rabbit and guineapigs. Camphor, picrotoxin, metrazol and strychnine were selected from different groups.

Methods

The dogs to be experimented upon were brought under laboratory conditions by keeping them for a few days under standard diet of rice 1½ ozs. and meat 2 ozs. The feeding was done only once in the day at 4 P.M. The experiments were mostly undertaken between 12 noon and 4 P.M. The dog to be experimented upon was weighed. About 10 c.c. of venous blood was collected in an oxalated tube for determination of blood sugar, urea and chlorides. Another 10 c.c. was taken out in a small conical flask containing a little soda citrate for blood calcium. The convulsant drug was then given, dose varying according to the weight of the animal. Blood was collected again after convulsions had taken place in fair numbers, usually after half an hour or so, after giving the convulsant. The following biochemical determinations were done:

(1) *Blood sugar.* This was done by Hagedorn and Jensen's method: 1 c.c. of oxalated blood is immediately deproteinised for fear of glycolysis. The protein-free filtrate which contains all the reducing sugar of the blood is heated with an alkaline solution of standard potassium ferricyanide. A part of the ferricyanide is thus reduced to ferrocyanide and the extent of this reduction indicates the concentration of sugar in the blood.

The estimation of potassium ferricyanide before and after treatment with the blood filtrate is carried out by treating it with an excess of potassium iodide and zinc sulphate in an acid medium and by titrating the iodine thus liberated against a standard solution of sodium thiosulphate. The zinc sulphate is added only to precipitate the potassium ferrocyanide as the double salt of potassium and zinc.

(2) *Blood urea.* This was estimated by Vanslyke's method: 3 c.c. of blood is treated with urease under standard conditions of pH and temperature. The urea of blood is thus converted into ammonium carbonate. A strong alkali is then added to decompose the ammonium carbonate into ammonia, which is carried over by a current of air into a measured volume of standard acid. The acid used up for neutralisation of the ammonia is a measure of the urea content of the blood.

(3) *Blood chlorides.* Firstly the proteins of the blood were separated by the method of Folin and Wu using sodium tungstate and sulphuric acid. The protein-free filtrate was estimated for chloride by the method of Whitehorn.

(4) *Blood calcium.* This was done by the method of Clark and Collip. Citrated plasma was used. Calcium was precipitated as oxalate. This calcium oxalate after washing was dissolved in sulphuric acid when it liberated an equivalent amount of oxalic acid which was then estimated by titration against a standard solution of potassium permanganate.

In every case two readings were taken and the mean noted as the result.

The following cytological determinations were done:

(1) *R.B.C. and W.B.C. counts.* Blood was taken when it was flowing freely from the needle puncture.

(2) *Hæmoglobin percentage.* This was estimated by Sahli's scale.

(3) *Differential count.* The types of white blood corpuscles vary slightly in the dog. The band form met with was counted as polymorph.

Observations

1. *Medullary convulsant*—Pictrotoxin was used. 0·75 mgm. of pictrotoxin per Kg. of dog's weight dissolved in 1 cc. of rectified spirit was injected intravenously. After about 5-10 minutes the animal vomited probably due to stimulation of the vomiting centre in the medulla. Typical clonic and irregular convulsions then started. Legs were adducted to the maximum, the back became concave, the animal seemed to rest on the abdomen. The fingers and toes were spread out showing the web. The animal tried to jump and turned somersaults. The convulsions were just like shivering fits. Four experiments were done on different dogs. The results are tabulated below:—

Read at the Scientific Section, XIX All-India Medical Conference, Patna, April 1943.

Dog No.	Sex.	Wt. in Kg.	R.B.C. in million	W.B.C. in thousand	Hb %	Blood sugar in mgm. %	Blood urea in mgm. %	Blood chloride in mgm. %
1	M.	12½	5·75 before.	9	75	115	40·5	542
			6·8 after.	12	87	221	48	552
2	F.	13	5·35 before.	11	65	105	33	560
			6·15 after.	15·83	75	244	37	586
3	M.	12¾	7·01 before.	14·69	67	89	27·5	563
			8·0 after.	45·63	78	212	30	573
4	F.	7	6·92 before.	37·5	64	97	59	572
			5·83 after.	42·5	72	203	63	592

Thus R.B.C. increased by about 1 million in most cases. W.B.C. count increased by 3000 to 5000. Hb percentage increased by 8 to 12. Blood sugar increased by 95 to 140 per cent. Blood urea increased by 8 to 19 per cent and chlorides by 2 to 4 per cent.

(2) *Spinal convulsants*—Strychnine was used. 0·25 mgms. dissolved in 1 c.c. of distilled water per Kg. of dog's weight was injected subcutaneously. Typical strychnine convulsions started in about fifteen minutes. They were tonic in type and explosive in character. There was a simultaneous contraction of most of the muscles of the trunk and limbs. The flexors and extensors contracted simultaneously. The trunk and limbs were extended rigidly. Three experiments on dogs were done. The results are tabulated below:

Dog. No.	Sex.	Wt. in Kg.	R.B.C. in million	W.B.C. in thousand	Hb%	Blood sugar in mgm. %	Blood urea in mgm. %	Blood chloride in mg. %
5	F.	20	5·63 before	9 ·8	68	134	38	532
			6·4 after	9 ·9	74	179	40	555
6	M.	10	4·48 before	14 ·06	71	106	33	541
			5·33 after	15 ·31	71	168	35	514
7	F.	8	4·48 before	20 ·0	54	114	31	495
			4·86 after	36 ·25	60	173	33	531

Thus R.B.C. count increased by about 1 million, W.B.C. count increased by 1000 to 1200. Hb per cent increased by 0 to 6. Blood sugar increased by 30 to 60 per cent. Blood urea increased by 8 to 10 per cent and blood chlorides by 2 to 5 per cent.

Discussion

The idea of the present investigations was to find out if the biochemical and other changes in blood with different types of convulsants were similar in nature and extent and to find out whether the type of changes occurring corresponded to the changes which give rise to convulsions in diseased conditions.

Different convulsants acting on different parts of the C.N.S. may send different sets of muscles into convulsions. The degree of muscular exertions may also differ. These factors may effect different biochemical and histological changes or aberration of stimuli may occur from one place to another in intact C.N.S. in which case the changes may be of the same nature but may differ in extent.

Picrotoxin which is supposed to act on the medulla as its effect vanishes when medulla is destroyed has caused during the postconvulsive stage rise in the blood sugar, blood urea and blood chlorides. Strychnine which is a spinal convulsant as shown by the fact that it is ineffective on destruction of the spinal cord has also caused a rise in all three *i.e.,* blood sugar, blood urea and blood chlorides. The difference between the action of the two is that blood sugar with picrotoxin was raised by 95 to 140 per cent while with strychmine 30 to 60 per cent. Again blood urea increased with picrotoxin by 8 to 19 per cent while with strychnine only by 8 to 10 per cent. Change in the blood chlorides was nearly the same in both. The greater changes in the case of picrotoxin may be explained by the fact that the stimulation of the medulla causes stimulation of all the motor fibres going to the face and body muscles while lesser changes with strychnine may be due to the fact that it probably does not stimulate the motor cells but somehow facilitates the reflexes and makes them abnormal *i.e.,* causes the contraction of both flexors and extensors.

The changes in R.B.C. and W.B.C. counts and Hb. percentage are probably due to leaking of the plasma out of the capillaries in convulsions due to dilatation of the vessels by the metabolites and partly due to the contraction of the spleen.

Conclusions

With both convulsants *i.e.,* strychnine and picrotoxin, blood sugar, blood urea and blood chlorides are increased and also R.B.C. count, W.B.C. count and Hb. percentage.

This is only a preliminary observation and no definite conclusions are possible on observations over few experiments. This work is being continued and detailed results along with the applied aspect will be published later.

Acknowledgment

The author wishes to express his thanks to Professors B. Narayana and B. N. Prasad of P. W. Medical College, Patna.

STANDARDISATION OF THE WASSERMANN ANTIGENS BY SELECTION AND CORRECTION

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This communication is consecutive to a previous communication entitled the titrated positive controls in the Wassermann reaction, in this journal (Greval, 1944) Only by the use of these controls can the selection or the correction of the antigens be made by a process which is measurable and, therefore, repeatable.

Information on two antigens not in common use has been included.

Selection of Alcoholic Heart Extract

Samples of McIntosh and Fildes' antigen may differ more amongst themselves, in potency, than from a sample of Bordet's cholesterinised antigen. The kind of the antigen is not so important as the quality.

The writer uses four antigens: (*i*) alcoholic heart extract uncholesterinised, (*ii*) the same extract cholesterinised (McIntosh and Fildes' antigen), (*iii*) the cholesterinised antigen also phenolised and (*iv*) Bordet's antigen cholesterinised. The first three are prepared from the same extract and the fourth from the same heart. For selection, therefore, the selection of the heart extract is enough.

The selection is made testing several heart extracts in a 1 in 15 dilution. A +++ serum should fix 4 MHD of a complement of optimal titre and reaction with a good heart extract in a 1 in 10 dilution completely (+) and a 1 in 20 dilution incompletely (T/±). The incomplete fixation should not be of a lower grade than the one given by the pooled extract in use at the time. The +++ serum when pooled in lots of 25 usually fixes 3 MHD of the complement with the cholesterinised antigen in a 1 in 50 dilution completely (+) and a 1 in 100 dilution incompletely (T or ±). The optimal titre of the complement is 1 in 40, 1 in 50 or 1 in 60. The optimal reaction denotes absence of 'shyness' or 'fastness' with cholesterin. The dose of 4 MHD is chosen to correspond to the 5 MHD of the Method No. 4 which uses cholesterinised antigen anticomplementary to the extent of 1 MHD: the heart extract not being anticomplementary, the 4 MHD does the work of 5 MHD.

The selected heart extracts are pooled in lots of six.

Cholesterinisation of the pooled extract in bulk yields a more standardised antigen than mixing of small quantities of the extract and cholesterol solution immediately before use.

Correction of Alcoholic Heart Extracts

Lots of 1·5 c.c. of the extracts not coming up to the standard by selection are concentrated in small measuring cylinders (capacity 10 c.c.) to 1·25 c.c. tested for absence of hæmolytic activity consequent on concentration and put up again in a 1 in 15 dilution with the +++ serum. 3 volumes of the 1 in 15 dilution should not hæmolyse 1 volume of 3% RBC. There may be no improvement in the fixation, the extracts then are rejected; there may be an improvement bringing the extract up to the standard, the total quantity of the extract then is concentrated in the proportion of 15: 12·5; or the improvement may fail to bring the extract up to the standard, a concentration of 15: 10 is then tried and the two tests repeated.

Bordet's Antigen

This antigen is the alcoholic extract of the acetone insoluble fraction of the heart muscle. Its preparation and use have been described in details previously elsewhere (Greval, Chandra & Das, 1939). It is also cholesterinised though the cholesterin content is low.

The writer makes this antigen only from the muscle (kept in acetone) which has yielded a satisfactory alcoholic heart extract without concentration. Its use being limited to one tube out of a batch of five, the quantity so prepared lasts as long as the other antigens.

One supposed advantage of Bordet's antigen is that, because of its low content of cholesterin, it is not anticomplementary. The writer does look upon this quality as an advantage. When used alone (as it has been in Calcutta for many years) it gives no indication of the quality of the complement although the fixation caused by it is affected significantly by the quality.

The antigen is more sensitive but not more specific than the McIntosh and Fildes' antigen. Further, it does not differentiate satisfactorily between early, late, treated and untreated cases of syphilis. The writer uses it for appraising doubtful reactions or even negative reactions with significant histories.

Phenolised McIntosh and Fildes' Antigen

This antigen is made from the cholesterinised alcoholic extract by diluting the latter with 14 parts of 25% phenolised saline (instead of plain saline). It is a little more anticomplementary than the unphenolised antigen and more sensitive. Its specificity is good and it differentiates between early, late, treated and untreated cases of syphilis. The writer uses it in clinically known cases only.

Summary

The Wassermann antigens can be standardised, by selection or correction, by the use of titrated positive controls only.

References

Greval, S. D. S.—*J. Indian M. A.*, **13**:107, 1944.
Greval, S. D. S., Chandra, S. N. and Das, B. C.—*Indian J. M. Research*, **27**:589, 1939.

(*Continued from page 145*)

involves the risk of increased manipulations causing liability to injury or infection of the mother: if the child dies and the aftercoming head has to be perforated the operation will be more difficult because of the position of the arm which cannot always easily be brought down by the method of reversed rotation and manipulation.

With the aid of the manikin and doll I shall desire now to demonstrate the alternative methods of rotation for your consideration, and to indicate the method of correction of single or double dorsal (nuchal) displacement of the arms. It will be noted that in the recommended method of rotation the process of disengagement is emphasised in order to avoid excessive twisting of the neck of the child.

In endeavouring to avoid the complication of extended arms, traction should be applied to the fœtus only when essential and to a minimal amount and along with the uterine contraction and may be supplemented by the judicious use of Kristeller pressure to augment the uterine power when necessary.

COMPLICATED BREECH PRESENTATION : MANAGEMENT OF EXTENDED ARMS

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Nowadays there is general agreement that breech presentation is an abnormality which is serious for both mother and child The importance and the frequency of this malpresentation has always drawn special study of its cause, its diagnosis and its treatment or management, and early references may be seen in the Hippocratic writings.

After centuries of observation and recorded thought it might be expected that on all leading points the rules for management would be standardised. It is pleasant to find that this is not the case, however, and in matters such as the conduct of the uncomplicated breech and the management of the cases of breech with extended legs interest is fresh today and discussion is often animated and agreeably stimulating and controversial.

My remarks this morning on a part of this subject concern cases of breech presentation in which no abnormality to cause the malpresentation is known to be present, and will be limited to a consideration of delay in the birth of the shoulders due to extended arms. This abnormality in the mechanism might, for example, come about during the vaginal delivery of a primigravida with a frank breech descending through a tight incompletely dilated birth canal so that the arms might become carried up into the extended position, or as another example when a leg has been brought down during version, the traction exerted to bring down the breech may promote extension of the fœtus and so lead to extension of the aftercoming arms, however much it might have been desired to avoid this complication of labour.

This situation will be recognised by noting immediately any delay in the birth of the shoulders and on passing a hand along the front of the fœtus the absence of the arms from the normal folded position will confirm the diagnosis. Proceeding at once to the delivery of the posterior arm, the legs of the child are taken in one hand and traction is made first downward so that the axilla may come into view, and then the child's legs are held forward to enable the operator's other hand to be passed into the hollow of the sacrum and along the side of the child until the first and second fingers come to lie alongside the child's elbow when pressure must be given to cause the elbow to flex and the forearm to pass across the face and then the arm to be brought down by drawing the hand outside. The body of the child is now lowered and an attempt is made to deliver the anterior arm with the same hand and in a similar manner. It is emphasised that during these manipulations the trunk must be drawn down sufficiently low for the lower angle of the scapula to be seen, if precise and prompt delivery of the arms is to be obtained, while at the same time the hold must be loose enough to permit the necessary manipulation.

Read at the Scientific Section, XIX All-India Medical Conference, Patna, April 1943.

In the event of delivery of the anterior arm not being possible it will be necessary to rotate the child so that this arm will become posterior and then by making use of the greater space in the hollow of the sacrum it should be possible to complete delivery of this arm fairly easily and quickly, provided that no new difficulty is encountered. It is, however, at this time that the serious difficulty of nuchal displacement is liable to arise and, therefore, the method of rotation is of great importance if this accident is to be avoided.

A case may be imagined where a primigravida with a half breech is received in labour and the legs have been brought down by Pinard's manœuvre on account of delayed progress, and then one arm has been brought down but rotation is required for access to the other arm. In such a case there will be concern as to the possible incomplete dilatation of the soft parts and perhaps some limitation of the capacity of the pelvis may be suspected so that the matter of prompt and gentle completion of the delivery is urgent and anxious. In these circumstances the occurrence of a nuchal displacement will be a most serious complication of the delivery likely to give dangerous delay and liable to lead to a broken humerus or clavicle or quite probably to the death of the child at a time when the greater part of its body has been born and is in the hands of the accoucheur. The thought of the humiliation and distress of such a situation may be a spur to further consideration of this matter.

The usual rule for rotation is that the body of the child which is slippery and greasy is grasped in a towel with two hands so that the anterior arm now becomes posterior. The movement of rotation should be made towards the side on which the back lies; if the child's posterior left arm has been brought down and the anterior right arm is extended the body should be rotated in an anti-clockwise direction towards the mother's right, and *vice versa*. This will avoid the risk of nuchal displacement and encourage folding of the forearm over the face where it will be more easily reached. During rotation traction should not be exerted lest the head be caught and twisted, but rather the rotation should be preceded by disengagement, and should proceed deliberately and gently but with precision to avoid delay.

This method is not universally taught and practised, and experience as an examiner has shewn that the instructions concerning rotation as set out by Eden and Holland in their Manual of Obstetrics are widely followed. The influence and authority of this textbook are deservedly high and the authors in describing their method of rotation point to the advantage they claim of keeping the occiput forwards, and moreover they claim that the likelihood of such an occurrence as nuchal displacement is extremely remote. The method of rotation advised in that textbook ignores the risk of dorsal (nuchal) displacement of the arm by turning the child in a direction away from its own back, and this is the shortest movement to bring the required shoulder posterior while keeping the back of the head to the front (avoiding a posterior position of the head).

I venture to disapprove of this method and disagree that the risk is remote. If nuchal displacement occurs, at best it

(*Continued on page 144*)

MEDICAL PREPAREDNESS SERIES*

TREATMENT OF BURNS IN GENERAL PRACTICE

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For obvious reasons, the subject is now one of real interest to the profession, and as such the general practitioner should be fully conversant with the management and practical handling of these cases. Burns and scalds need not, from this point of view, be dealt with as separate entities.

The methods of local treatment that have been enthusiastically advocated are legion. A general practitioner, therefore, is apt to get perplexed with the long list of methods recommended. I shall here deal with the parent technique of Tannic Acid Eschar and its modifications, as well as other methods that have gained popularity in recent years.

Classification

For practical purposes, burns are classified clinically as (1) Minor cases (usually ambulant) and (2) Major cases.

Minor cases are those that are usually only of the 1st and 2nd degree, not involving more than one-tenth of the total body surface and without producing marked shock. These cases also exclude burns in special sites such as face, neck, hands, flexures and perineum.

Major cases are extensive burns involving more than one-tenth of the body surface and also include burns of the second and third degree, of special sites mentioned above.

Prognostic Considerations

It is the extent of the area affected rather than the depth of the burns that determines the seriousness of the issue. An affection of more than one-fourth of the total body surface specially with burns of 2nd and 3rd degree is a matter of grave import. Burns of the trunk, specially in front, and of the face are of the worse prognosis than those of the limbs. Those of perineum and genitalia are difficult to manage on account of contamination by natural discharges and supervention of sepsis. Infants and children, as well as the aged react unfavourably to burns. Burns affecting hands and flexures of joints are notorious for developing disabling contractures. Face burns may involve the eyes directly or may lead to subsequent complications by producing ectropion. Burns of the neck may produce gross deformity (torticollis) or involve the larynx, trachea and other structures in progressive strangulation by scar formation and contracture.

Clinical Course and General Pathology of Burns

The clinical features usually appear in the following sequence of stages in most cases of extensive burns, specially those involving the trunk and face:—(*i*) Primary shock, (*ii*) Secondary shock, (*iii*) Toxæmia, (*iv*) Sepsis and (*v*) Healing.

Primary Shock (*neurogenic*): Primary shock follows dramatically soon after injury, though uncommonly it may be very mild, even in extensive cases. It resembles a vasomotor attack with a slow or normal pulse, pallor, sweating, sub-normal temperature and low blood pressure. Recovery is usual, mortality being less than 3 per cent unless complicated by asphyxia.

Secondary Shock (*oligæmic*): It is a serious condition, usually coming on after recovery from the primary stage or may merge into it. It develops insidiously within 3 to 6 hours of the accident reaching its greatest intensity within the first 24 hours and is characterised by a profound fall of blood-pressure, a quick thready pulse, thirst and restlessness, occasional vomiting and increased hæmoconcentration due to immense loss of plasma in and subjacent to the burnt surface. It is believed that 60 to 70 per cent of deaths from burns occur at this stage.

Stage of Toxæmia: It usually ensues within 12 to 60 hours from the time of injury and may supervene upon the stage of secondary shock. Clinical signs are: vomiting, listlessness, cyanosis, hyperpyrexia (103° to 105°F) followed by signs of circulatory collapse, with a rapid feeble pulse. The nature of the toxin remains debatable. About 15 per cent of deaths are said to occur at this stage.

Stage of Sepsis: This is related directly to the depth of the burn as well as the efficiency of the local treatment adopted and the general power of resistance of the patient. It has been known to develop fulminantly even under a well-formed eschar.

Stage of Healing: This is either short or more prolonged depending upon the degree of infection of the wound, the depth of burn and the general condition of the patient. Cases of partial skin destruction heal rapidly, epethelization occurring from little islets or undamaged epidermal remnants as well as from the margins of the wound. Areas of total skin destruction unless treated by well-planned skingrafting, terminate in fibrosis and contracture.

It will be convenient to summarise at this stage the more important causes of death from burns. They are:—(*a*) Asphyxia, (*b*) shock (primary and secondary), (*c*) anærobic infection and sepsis, (*d*) fat embolism, (*e*) lung complications, (*f*) nephritis, and (*g*) acute enteritis (toxic diarrhœa) and duodenal ulcer (curling).

Treatment of Burns

Minor Cases—Rest, relief of pain and prevention of infection are the principles involved. Thorough preliminary cleansing, if necessary under general anæsthesia (preferably gas and oxygen) is undertaken with due aseptic precautions. The part may be dipped in warm saline and adherent bits of burnt clothing carefully removed. Ether, soap, benzene or sodi bicarb solution should be used if the part is soiled with grease. Blisters should be laid open and epidermal tags snipped off. The part may then be dusted over with sterilized sulphanilamide powder or painted with 1/1000 acraflavine solution. Gentle handling is essential. Undue exposure should be avoided.

Local Treatment—Tannic acid, merthiolate or gentian violet jellies, Burnol, codliver oil or sulphonamide glycerine

* This is the tenth of a series of articles on war medicine, A.R.P. and allied subjects which are being published from May, 1943.—Editor, *J. Indian M. A.*

paste are the remedies commonly used. These are applied with 2 or 3 layers of sterile gauze dressings and bandaged over. When nothing is at hand freshly prepared warm infusion of tea or white of eggs may be applied over the burnt surface, to be followed by local treatment on lines suggested as soon as possible. Dressings should only be removed if soaked with discharge and new dressings re-applied. Healing is usually complete within a fortnight in the absence of secondary infection. 1,500 units of tetanus anti-toxin, as a preventive, should be administered in all cases of burns, preferably in 2 doses at a week's interval.

MAJOR CASES—The treatment resolves itself into: First aid treatment and final treatment including treatment of complications.

First Aid Treatment—This is directed to the cure of asphyxia, the treatment of shock and prevention of infection while arrangement for transport of the patient to hospital is being made.

In major cases, it is inadvisable to indulge in local treatment in a first-aid post. Tannic acid, silver nitrate and other coagulants, as well as oily preparations should be avoided as they hinder final treatment. Clothes, unless grossly soiled, should not be removed. The first-aider should only cover up the affected areas with clean dressings, administer first aid treatment for shock and transport the patient to the nearest hospital or treatment centre at the earliest opportunity.

Final Treatment—Patient is put to bed with the foot-end raised and is kept warm under an electric cradle covered with blanket (Tem. 85°-88°F). Hypodermic injection of morphine is administered with due regard to age and any previous dosage received by patient (usually gr. 1/3 to gr. 1/2 for an adult). Tr. opii in regulated doses is preferable with infants and young children. Half-hourly record is kept of temperature, pulse, respiration and blood pressure. It is inadvisable to undress the patient or start local treatment until shock is well under control. If able to swallow, hot drinks are given freely, preferably mixed with glucose, otherwise, continuous rectal drip saline is administered.

Patient usually rallies from primary shock with sedatives, warmth and restoratives mentioned but in severe secondary shock one is faced with a major problem. Oxygen should be administered freely through a B.L.B. mask if available and no time should be lost in replacing fluid loss and restoring hæmoconcentration and blood pressure.

It is now universally recognized that those who have lost blood need blood, those who have lost plasma need plasma and those who are merely dehydrated need saline. Plasma and serum transfusions are preferable to blood transfusion for treating shock associated with burns.

No preliminary grouping is required with plasma as with whole blood transfusion. Whole blood on account of cellular content fails to diminish appreciably hæmoconcentration and viscosity of blood and may, therefore, be definitely harmful. Plasma moreover, can be stored in large quantities and practically never gives rise to untoward anaphylactic reactions in shocked cases.

If plasma is not available, gum-saline or glucose-saline should be administered by the drip method. To maintain the chloride balance of the body administration of 1000 c.c. of isotonic sodium chloride daily in an adult is necessary. Intravenous injections of glucose and sodi bicarb is further helpful in controlling acidosis and liver damage.

Atropine sulphate gr. 1/100 should be administered before and after transfusion.

The amount of fluid to be transfused can be judged fairly accurately by nothing the general improvement of the patient clinically and the rise of blood pressure level. A rough and ready method for the general practitioner is to study the hæmoglobin percentage before and after the transfusion and a sufficiency is indicated when the hæmoglobin percentage gradually falls to about one hundred.

Adrenal cortical extract (desoxycorticosterone acetate) in 5 mgm. doses intramuscularly every 2 hours in adults has been found to be very useful in combating shock.

Local Treatment—Only after the patient has rallied from shock should preliminary cleansing be undertaken under general anæsthesia (gas and oxygen, if available) with full surgical aseptic technique and with meticulous care, avoiding rough handling, undue exposure and undue rubbing of the affected parts. Loose tags and blisters should be snipped off and oil or grease removed as previously indicated.

Local application: The object of local application is to form an eschar which has the following advantages:—It relieves pain, arrests loss of serum, minimises dehydration, and loss of body heat from the surface, diminishes toxæmia by coagulating the tissues and absorbing and fixing the toxins produced locally, prevents infection of the wound and encourages rapid healing under a scab. It also does away with the need for repeated painful dressings.

Tannic acid & silver nitrate: Aqueous solution of tannic Acid is sprayed on either with an atomizer or a spray or applied as a compress soaked in sterile gauze. The strength of the solution used varies from 2 to 20 per cent. Stock solution of tannic acid deteriorates on keeping, with the formation of pyrogallol derivatives. To prevent this a fresh solution should be made out of powder kept in stock and made up as follows:—Tannic acid gr. 17½ and perchloride of mercury gr. ½. This when mixed with 2 ozs. of sterile warm water yields a 2 per cent tannic acid solution with 1/2000 perchloride of mercury. Tannic acid solutions of weaker strengths *e.g.*, 2 per cent or 5 per cent are sprayed on every half an hour under an electric cradle, or more rapidly dried by a current of hot air from a hair-dresser's blower. A firm black coagulum results in about 2 to 3 hours which remains in position for 7 to 21 days in the absence of infection. Strong solution of tannic acid, *e.g.*, 20 per cent, forms a rapid scab but the coagulum is not so thorough as with the weaker strengths. Besides, it cracks easily and tends to give rise to subjacent infection. Sterilized sulphanilamide powder or gentian violet (10 per cent should be applied to the cracks to prevent infection. The coagulum should be inspected several times daily from this point of view. When the trunk is burnt both in front and behind, the patient should be made to lie on sterilized towels, preferably treated with acriflavine, and change of posture should be performed gently. If infection supervenes the scab gets lifted up which should then be removed, the area painted with acriflavine or gentian violet and a fresh eschar reformed over it or alternatively the Triple Aniline Method, described later, should

be adopted. Tannic acid with 5 or 10 per cent silver nitrate solution or with 1 per cent gentian violet or acriflavine (1 in 1000) has been tried with great success in war burns. The latter is said to do away with the necessity of preliminary cleansing of the burnt areas on account of its antiseptic property.

Very rapid tanning can be obtained by combining tannic acid with 10 per cent silver nitrate, the coagulum then forms "within minutes instead of hours"—a matter of extreme importance in treatment on mass scale.

Tannic acid treatment outside the areas of the extremities and flexures and face still remains the treatment of choice in general practice, provided the preliminary cleansing is done with meticulous care and the wound is treated with sulphanilamide powder or painted with gentian violet or acriflavine before tanning. It has, however, a tendency to produce excessive scar formation and contracture and is, therefore, not a favourite application for the special regions mentioned above. Gangrene with dropping off of fingers and toes has been known to follow local treatment with tannic acid.

Sulphanilamide Treatment of Burns: After preliminary cleansing the burnt surface is sprinkled with sterile sulphanilamide powder and then covered with Tulle-grass, over which several layers of gauze soaked in normal saline are retained with bandage. The gauze dressings are removed and reapplied leaving Tulle-grass *in situ*. Epithelisation takes place under the Tulle grass which acts as protective.

Glycerine Sulphonamide Paste (Euglamide): The paste consists of soluble sulphonamide (Albucid), glycerine, kaolin and codliver oil. It induces rapid healing of burns complicated by sepsis.

Triple Dye Method: Gentian violet 1/400, brilliant green 1/400, neutral acriflavine 1/1000. This may be applied as a paint over the burnt areas. Repeated applications are required for suitable coagulum to form. The method is rapidly gaining popularity on account of the rapid healing that it induces and the tendency to lessened scar formation and contracture.

Bunyan's Envelope Method: A method of intermittent irrigation (with 5 per cent electrolytic sodium hypochloride solution) of the burnt surface isolated in a specially made water tight envelope. It requires an efficient nursing staff and is unsuitable in general practice.

Burns in Special Sites—*Face*: Eyes should be protected by instilling liquid paraffin and covered with vaseline pads. Sulphonamide paste, codliver oil or triple dye method should be used.

Hands and fingers: There is no unanimity yet with the choice of local application. Sulphonamide paste, aniline dyes, codliver oil and saline baths are the methods recommended. The hand fingers must be properly splinted to prevent deformities and the fingers kept abducted by packing gauze dressings at the webs between the fingers. Active movement should be encouraged to restore function after healing has made progress.

Perineum and buttocks: Treatment becomes difficult on account of soiling with natural discharges and consequent risk of infection as well as on account of nursing inconvenience. Children are best treated in gallows position and adults lying on the face with legs abducted—ankles secured by tying with the corners of the bed. Local applications recommended are the same as for treatment of the face.

Other regions: When the extremities are involved, the posture to be adopted and maintained, if necessary by splinting, will depend on the sites affected. When the flexures are affected, the joints should be kept in extension and *vice versa*. If both surfaces of a joint are involved then neutral position will be the best. If however, arm and fore-arm are both extensively burnt, 135° at the elbow with the fore-arm in mid-prone position is advisable. If the axilla is involved the arm should be maintained in the Policeman's 'Stop' position.

Plaster Casing in Cases of Burns: Burns complicated with injuries such as fractures of limbs should be treated by attending the burns first and then putting up the limb in plaster including the dressings. It ensures rest, encourages healing and also allows transport of patient which may be essential under war conditions.

Surgical measures: Amputations of extremities and digits, badly burnt and with little prospect of functional recovery, may be indicated in cases where sepsis has supervened. This has cut short the period of suffering in many well selected cases.

Skin-Grafting: A well planned skin-grafting effectively curtails the stage of healing and materially diminishes scarring and contracture. It is specially indicated in all burns deeper than third degree, where islets of epidermal remnants are few. It is also indicated where the ulcer becomes callous and epithelization from the margins scanty. In burns complicated by sepsis skin-grafting is useless until the infection is brought under control. Compress with hypertonic solution of sodi-sulph or 10 per cent sodium chloride solution or with a mixture containing one part of eusol, 60 parts of glucose and 10 parts of glycerine is helpful. Pinch grafts are, in general, better than Thiersch's grafts, although the latter may be used over granulating surface of deep wounds. Graduated doses of infra-red or ultra-violet rays stimulate healing. An elastoplast dressing also accelerates epithelization.

Diet: Easily digestible, of high calorific value and rich in iron, sulphur, calcium and vitamins. It should also contain adequate quantities of sodium chloride, glucose and salts.

Phosphorus Burns

Phosphorus is contained in certain bombs as incendiary filling, particles of which may become embedded in the skin as a result of explosion. The particles continue to burn unless rapid action is taken. The part should immediately be dipped in water and then into a solution made up by adding a table spoonful of sodium carbonate to a tumbler of warm water, or the burnt area may be covered with a gauze pad soaked in 2 per cent solution of copper sulphate. The chemicals neutralise phosphoric acid and render the superficial part of the phosphorus comparatively innocuous. The particle then may be removed with forceps. Oily dressings should never be used as phosphorus is readily soluble in oils. The ulcerated areas may then be treated with coagulants or antiseptic ointments as previously described or with a soothing ointment containing MgO_2 (heavy), borax, sodi-bicarb and starch.

CASE NOTE

PNEUMOTHORAX CAUSED BY ANAEROBIC GAS-FORMING ORGANISMS*

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Cases of gangrene of the lung have been reported from time to time and some of them have terminated in pyopneumothorax; but infection of pleural fluid by anærobic gas-forming organisms is very rare. The case which is being reported below is still more rare and interesting from the point of view that no penetrating injury of the chest of any kind occurred before the infection took place. So, clinically the source of infection is very uncertain (idiopathic).

Report of the Case.

P. M., aged 18 years, Hindu male, was admitted to the Guzri Ward of the Patna Medical College Hospital on 23-10-42, complaining of pain on the left side of the chest, mild fever and dyspnœa. He gave history that he had developed this pain on the chest after an exposure about a week ago and had irritable cough. Patient was a victim of epileptic fits, and his elder brother had been suffering from tuberculosis of the hip joint.

24-10-42—The base of the left lung behind showed evidences of diminished vocal fremitus and vocal resonance with a dull note on percussion. The apex beat was displaced towards the right. Heart sounds were fairly strong, pulse rate 84 p.m., respiration rate 24 p.m. Epileptic fit at 10-30 a.m. Clinical diagnosis was pleurisy with effusion (left side).

27-10-42—The temperature shot up with rigor to 104°F Blood film showed no M.P.

29-10-42—Pulse rate 130 p.m., respiration rate 36 p.m.; temperature 103°F; patient still complaining of pain on the left side of the chest specially in the precordial region. Vocal fremitus and vocal resonance markedly increased in the left precordial region, tubular breathing in the left precordial region, no other abnormality was detected clinically. *Total W.B.C.* count was 20,973 per c.mm. *Urine* examination showed absence of albumen, sugar and acetone. *Sputum* did not reveal any acid-fast bacilli.

Clinically it became quite evident that the rise of temperature was due to bronchopneumonia complicating pleurisy with effusion.

3-11-42—The general condition of the patient deteriorated, the temperature ranged between 103° and 104°F. Pulse and respiration rates were rapid and there was extreme breathlessness. Paracentesis thoracis was done and a thin blood-tinged foul-smelling pus came out with bubbles of gas.

4-11-42—The patient developed cellulitis around the site of puncture on the chest.

5-11-42—Pathologist's report on examination of pleural fluid: Microscopic—Pus cells present (a few). Numerous Grampositive bacilli and streptococci present. Culture—No organisms isolated in ærobic culture. In anærobic culture Grampositive spore-forming bacilli and streptococci isolated.

6-11-42—1-30 a.m. The patient had developed acute pneumothorax.

7-11-42—A sinus has formed at the site of puncture. Blood culture sterile up to 72 hours.

11-11-42—The patient expired at 10-45 a.m.

Discussion

It seems that the patient suffered from dry pleurisy in the beginning, then developed effusion on the left side of the chest and a part of the left lung got consolidated which subsequently terminated in pyopneumothorax.

The point of interest in this case was to find out the source of the gas and also to trace out the route of infection. There can be two possibilities:—(*i*) Infection of the pleural fluid after some penetrating wound of the chest—this is ruled out by the history. (*ii*) Gangrene of some thoracic viscera spreading to pleura.

The latter hypothesis is more probable as 'the pleura is almost invariably affected when the gangrene reaches the surface'.

The gas in the pleural cavity could only either be due to the anærobic gas-forming organisms or that perforation occurred giving rise to fetid pyopneumothorax—the latter being common in such conditions; or may be due to both factors acting conjointly.

Taking into account the observations at the time of paracentesis thoracis it seems that a part of the gas was produced by the gas-forming anærobic organisms; while the sudden development of restlessness at 1-30 a.m. on 6-11-42, and detection of clear evidence of pneumothorax indicate that the rupture of the pleura occurred with sudden inrush of air which caused distress, so it is evident that if the gas-forming organisms were solely responsible for the pneumothorax then there would have been no sudden distress, besides no signs of gas in the thoracic cavity were clinically detectable till 1-30 a.m. on 6-11-42.

Vigorous treatment with sulphapyridine by injection, supplemented by oral administration was started, going up to 5 gm. on the 7th and 8th hospital days and little less on the subsequent days (based on a clinical diagnosis of bronchopneumonia). The temperature went up to 104°F. with rigor on 3-11-42 giving a suspicion of pyopneumothorax when the paracentesis thoracis was done and the blood-tinged foul-smelling pus with bubbles of gas gave some clue to the exact diagnosis which was later supplemented and supported by the pathologist's report.

As stated above a spreading cellulitis developed around the site of the puncture. This could be arrested with difficulty by giving adequate doses of anti-streptococcal serum and antigas-gangrene serum and sulphapyridine tablets and injections in heavy doses but a sinus resulted. The inevitable, however, happened and the patient collapsed at 10-45 a.m., on 11-11-42, the 20th day in the hospital.

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* Read at the Scientific Section of the XIX All-India Medical Conference, Patna, April, 1943.

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INDIAN MEDICAL ASSOCIATION

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INDIAN FISH LIVER OILS

Undernourishment is a common condition in this country. While everybody will agree that the main deficiency is in essential foodstuffs, vitamin deficiency also plays a large part. Vitamin A and D deficiencies figure prominently in this. The natural sources of these vitamins such as fresh milk, eggs, butter, etc., are not consumed in enough quantities due to poverty and ignorance. As a result, vitamin A deficiency is most widespread in this country. Keratomalacia is very common and xerophthalmia, phrynoderma also have a high incidence [1, 2, 3, 4]. Vitamin D deficiency is more marked in Northern India and Kashmir. Rickets in all forms and stages, and osteomalacia are common and even endemic in the upper part of Kangra valley. An unbalanced diet combined with lack of sunlight is the cause.

In peace time India used to import anually over 100,000 lbs. of fish liver oils. These were mainly used in prescriptions, proprietary medicines and tonics to combat the deficiencies. With this World War II this import has gradually stopped. The source of cod-liver oil in Norway is now cut off. Newfoundland, Faroe islands, etc., are too far away for easy and safe transport. Other countries cannot export cod-liver oil for reasons of national health during the period of war, if there is not enough surplus. Simultaneously increasing restrictions are being enforced against import in this country. Special licenses are enjoined for all drugs which come under that group "whose importation can be reduced without much difficulty". The net result has been that like many more imported drugs, cod-liver oil is not available in open market. It is now *openly* black-marketed with increasing adulteration. Mukerji and Iyenger[5] analysed 98 samples of medicinal cod-liver oil and its preparation for their purity and vitamin A content. These samples, with both foreign and indigenous labels, were obtained from civil hospitals, customs department and open market in different provinces of India. 59 samples (60·27 per cent) out of them failed to satisfy the B.P. requirements. 24 samples were found to be deficient in vitamin A and 4 samples out of this group were completely devoid of vitamin A. This situation must have further deteriorated during the following years. So it has been necessary to look for sources in home market. Vitamin A for its more widespread deficiency and being essential for growth and anti-infective properties, is more important. Fortunately, its source is abundant in this country. Indian fresh water fishes[6] yield liver oils very rich in vitamin A, *e.g., Air* (Mystus macrones), *Bhal* (Wallago attu), *Bhetki* (Lates calcifer), *Dhain* (Silonia siluroid), *Mrigal* (Cirrhina mrigala), *Pangash* (Pangasius pangasius), *Shole* (Ohiocephalus stratus) and *Shillang* (Silonia silompia). Among the sea fishes, the shark yields a liver oil which is 5-25 times richer in vitamin A than good cod-liver oil. In the month of February the liver oil of *Air* (Mystus macrones) has a vitamin A value of 44,800 international units per gram[7]. The hammer-headed shark (Zagaena Blochi) liver oil has a vitamin A value of 20,000 international units per gram[8] in comparison to 800 international units of Norwegian cod (Gadus callarius) liver oil. For industrial purposes it may be difficult to procure fresh water fishes in large number immediately. But the Indian Ocean is almost infested with sharks and they have more vitamin A in their liver oil than the cod fish. The Madras Government (Dept. of Industries, Commerce and Fisheries) is manufacturing shark liver oil in large quantities. But this is not enough. This should be emulated by other provincial governments bordering the sea or our industrialists. A market already exists and it is up to them to exploit the resources and make it available even to the poor.

Vitamin D content of Indian fish liver oil has not been studied so thoroughly. Every effort should be made to find out a fish whose liver oil has a high vitamin D content More fresh milk, eggs and butter should be consumed in areas where rickets and osteomalacia are present. Housing conditions have to be improved so that fresh air and sunlight may have access. The question of irradiation of yeast and Indian fish liver oil to increase their vitamin D content should be seriously investigated further. The preparation of synthetic vitamin D is not difficult. A good scope remains for its commercial development.

STERILISATION OF SULPHONAMIDE POWDER

With continued observation, both experimental and clinical, the sulphonamide group of drugs have been found not only efficacious in various infections of internal organs but it has also been found effective when used locally such as in the treatment of wounds. Goodman[1] thinks that their value in local use is difficult to exaggerate. Colebrook and Francis[2] have successfully used them in wounds infected with streptococci. It has also been used in prophylaxis of gas gangrene. Robson and Wallace[3] have used them for local treatment of burns. And extensive use of these drugs is being made in war wounds with more or less successful results. But

[1] Aykroyd, W. R. and Krishanan, B. G.—*Indian J. M. Research*, **23**:741, 1936.
[2] Aykroyd, W. R. and Rajgopal, K.—*Ibid*, **24**:419, 1936.
[3] Nichols, L.—*Indian M. Gaz.*, **68**:681, 1933.
[4] *Idem—Ibid*, **69**:241, 1934.
[5] Mukerji, B. and Iyenger, N. K.—*Transactions of the Medical College Reunion*, Calcutta, **2**:69, 1938-1939.
[6] Ahmad, Bashir—*J. Indian M. A.*, **10**:3, 1940.
[7] Seshan, P. K.—*Indian J. M. Research*, **27**:711, 1940.
[8] De, N. K., Majumdar, B. N. and Sundararajan, A. R.—*Ibid*, **26**:435, 1938.
[1] Goodman, L. S.—*Bull. New York Acad. Med.*, **18**:112, 1942.
[2] Colebrook, L. and Francis, A. E.—*Lancet*, **1**:271, 1941.
[3] Robson and Wallace—*Brit. M. J.*, **1**:469, 1941.

these drugs have got some limitation in their topical use due to their inactivation in presence of pus and other tissue fluids.

The topical use of these drugs have recently got a set back after publication of a report of a fatal case in the *Pharmaceutical Journal*[4] and an annotation[5] on the inquest of death published in *Lancet*. This was a case of a woman, who was operated on in a London hospital on April 13, 1942 for some gynæcological trouble. An widespread pelvic infection was discovered and free pus was found in the abdomen. The abdomen was swabbed dry and sulphapyridine powder was sprinkled on the operation area in the pelvis before the abdomen was closed, a rubber drain being left in. The progress of the woman was satisfactory for seven days, when she discovered that she could not open her mouth. Tetanus was diagnosed and 280,000 units of anti-tetanus serum was administered but she died on the next day. Postmortem examination showed infective process at the site of the operation in the pelvis and *Clostridium tetani* was cultivated from the operation site. Catgut used gave negative results and the organism was grown from the carton of the sulphapyridine powder used. Forgan[6], the medical consultant of May & Baker, Ltd., said in the inquest that while M. & B. 693 might be used topically, it was not recommended by the makers for use in a septic wound as pus inactivated the drug. This case report together with this declaration of Forgan should make one think twice before using this group of drugs topically.

In the meantime, the Food and Drug Administration of U.S.A. instituted an inquiry into the bacterial contents of the commercial sulphonamide dusting powders. Results were appalling[7]. The investigation showed that about fifty per cent of the commercial samples were contaminated with bacteria like staphylococci, stretococci, diphtheroids and both ærobic and anærobic sporeforming organisms. In an wound where the tissues are naturally devitalised, these bacteria add unnecessary hazards and there are always chances of tetanus and gas gangrene being developed. The investigators, therefore, tried to find out the results of implantation of tetanus spores along with the sulphonamide group of drugs in experimental wound infections in guinea-pigs. The preliminary experiments with 20 animals and final experiments on 70 guinea-pigs showed that not only does the drug fail to control the local infection but enhances the action of the spores by locally devitalising the injured tissues. So the Administration insisted that all suphonamide powders for local use marketed in U.S.A. should be properly sterilised and must not contain any contaminating oragnisms.

This finding has been supported recently by Fisher and others[8] who observed, after elaborate experiments both by cultural and animal inoculation methods, that "Five per cent sulphanilamide, sulphathiazole, or sulphadiazine ointments in a water dispersible base may become contaminated with disease-producing organisms which these drugs are not capable of killing." They have found that addition of oxidising agents like urea peroxide in up to 1 per cent concentration may help these drugs to overcome this difficulty. And they concluded that "These findings emphasise the importance of care in the manufacture of sulphonamide products intended for topical application. The addition of an antiseptic to enhance the bactericidal properties and insure sterility of sulphonamide ointments is indicated to be essential as a factor of safety."

The Medical Research Council of Great Britain called a conference to consider the matter[9]. This was attended by clinicians, bacteriologists and representatives of the Associations of British Chemical Manufacturers. They arrived at a definite conclusion on the point of sterilisation of sulphonamide powders both in a large and a small scale which is reproduced elsewhere in this issue[10].

This account will give our readers some idea of the problem of using a new drug too enthusiastically specially in India as we are in a definite mess so far as control of drugs is concerned. The much-wished drug bill has come but no action is being taken by the government as yet to ensure standardisation of drugs for public consumption.

We cannot be sure of the drugs we are using regarding their potency, suitability and sterilisation. The methods of sterilisation advocated by the British Medical Council is surely within the reach of any well-equipped hospital. But it is definitely beyond the scope of a general practitioner. The only other way to avoid in our country the occurrence of such a calamity as reported above is to market the powders in a properly sterilised container.

[4] *Pharmaceutical Journal,* **148**:192, 1942.
[5] *Lancet*—Annotations, **1**:770, 1942.
[6] FORGAN, R.—Reported in *Pharmaceutical Journal (loc. cit.).*
[7] WELCH, H. AND OTHERS—*J.A.M.A.,* **120**:361, 1942.
[8] FISHER AND OTHERS—*J.A.M.A.,* **122**:855, 1943.
[9] *Brit. M. J.,* **1**:263, 1943.
[10] *J. Indian M. A.,* **13**:153, 1944.

NOTICE

Capt. K. L. Saha, M.B., has offered a gold medal for the best paper on any subject in Pharmacology to be read at the 1944 session of the All-India Medical Conference.

Research workers and investigators who intend to submit a record of their work on this subject, are requested to send six typed copies of their articles to the Hony. General Secretary, Indian Medical Association, 23, Hindusthan Buildings, Calcutta, so as to reach the latter by the 30th September, 1944.

16-12-1943.

P. B. MUKERJI,
Hony. General Secretary,
Indian Medical Association.

CURRENT MEDICAL LITERATURE

MEDICINE

Blood Pressure in the Aged*

Russek (*Am. Heart J.*, July 1943) reports on the study representing a statistical analysis of the blood pressure levels of 1,000 retired seamen between the ages of 60 and 95 years. It was concluded that average systolic pressure and pulse pressure increase appreciably with age, whereas average diastolic pressure shows little variation after the age of 65 years. The incidence of "normal" blood pressure (150/95 or less) falls markedly with age. Less than half of the subjects fell in this group. Normal systolic pressure shows an increase with age, regardless of whether the upper limit is set at 150 mm. or at any figure below this level. All levels within the range of normal seem to participate in this change. Normal diastolic pressure shows a tendency to fall with age, and the number of subjects with low diastolic pressures (70 mm. or less) increases correspondingly. Arteriosclerosis not only increases the incidence of systolic hypertension with age, but also produces an increase in pulse pressure among subjects with normal blood pressure. More than one-quarter of all the subjects and more than one-third or those over the age of 75 years had systolic hypertension. A study of the ratio of actual to expected mortality revealed that the life expectancy of those with systolic hypertension was of the same order as for those with normal pressure. Diastolic hypertension, on the other hand, carries a much more unfavourable prognosis. The life expectancy in this group was related to the diastolic, rather than to the systolic, pressure. The incidence of diastolic hypertension increases more slowly with age; it was found in less than one-quarter of the entire group. Normal, as well as average diastolic pressure, was comparatively low, and it would seem that the upper limit of normal has in the past been set at too high a level. The clinical course and life expectancy of patients with systolic hypertension strongly suggest that the latter originates as such, and has its own distinct mechanism. For practical purposes, the clinician may regard systolic hypertension in the aged as 'normal'. Future study of the nature of atherosclerosis may reveal that it is physiologic in old age. Finally, if 120 mm. represents the "true" upper limit of normal at any age, only 13 per cent of this group could be classified as normal.

Vasomotor Disturbances in the Hand after Injuries of Peripheral Nerves

Richards (*Edinburgh M. J.*, **50**:449, 1943) observes that after division of a peripheral nerve the vasomotor state of the denervated area passes through two phases: (*a*) an initial phase of vasodilation due to the interruption of sympathetic vasoconstrictor fibres (the warm phase) and (*b*) a second and permanent phase in which the temperature of the area approximates to that of its environment (the cold phase). There is no clear-cut distinction in time existing between these two phases and the factors responsible for the change from the warm to cold stage are not fully understood. The digit which is incompletely denervated may show almost normal reflex vasomotor activity. A completely denervated digit will not respond reflexly to changes in body temperature but will respond to the local metabolic needs of the tissues.

Adenylic Acid in the Treatment of Agranulocytosis and Mucous Membrane Lesions

Ruskin (*Am. J. Digest. Dis.*, **10**:81, 1943) writes that mucous membrane secretions can be viewed as an organic outer layer, noncellular in character, similar to the cellular cuticular layer of the skin, rather than as a foreign body extruded as a waste product and it forms as such an essential component of the mucous membrane. The study of this secretion shows it to be made up of mucin which is a relatively inert material and nucleoprotein which, however, is vital and can precipitate some bacterial toxins as well as actively inhibit bacterial growth. The significance thereof of nucleic acid in normal mucous membrane health leads one to a regard for its importance in the occurrence of lesions of the mucous membrane and explains the underlying mechanism for the improvement clinically of mucous lesions under vitamin B (yeast) therapy and the occurrance of the lesions in B avitaminosis. Thus B avitaminosis doubtless also represents nucleotide defiicency. The nucleotides which are four in number are united together to form the single molecule of nucleic acid which occurs chiefly in the cell nucleus and since it is composite of a nitrogenous base, a ribose sugar related to riboflovin and phosphoric acid, it constitutes the bulk of the non-protein nitrogen of our food. Of the four nucleotides two adenine and guanidine are purines and act as stimulant and diuretic. This group stimulates reticuloendothelial system, increases coronary circulation, participates in carbohydrate metabolism and muscle metabolism, acts as coenzyme and as glandular stimulant. The other two nucleotides are of the pyrimidine group and are depressant. This group precipitates toxin and binds toxalbumin, induces leucopenia on injection, inhibits bacterial growth and acts like barbiturate on metabolism. In considering nucleic acid metabolism one must recognise two possible mechanisms as occurring: one is the loss of nucleic acid in neutralization of toxins such as occurs in the reactions to infections like diphtheria, typhoid fever, scarlet fever; the other is an imbalance in nucleic acid occurring through the upsetting of equillibrium between the two antagonistic elements in nucleic acid, the prurines and pyrimidines. Continued administration of barbiturates is equivalent to feeding pyrimidine without the balancing pruines and in such cases one gets promptly in addition to hypnotic effect marked leucopenia, dry redness of the mucous membrane, rash and high fever like the exanthemata. Some of the cases of agranulocytic angina following barbiturates respond promptly to the use of pentose nucleotide which is the trade name of the mixture of adenylic and guanilic acid or to leucocyic extract or whole sedimented leucocytes. For guanilic acid there is still no demonstrable evidence of specific physiologic action. The adenylic acid element has been intensibly studied and it alone has on occasion sufficed in the treatment of agranulocytic angina. In dealing with

*Abstract through courtesy of the United States Office of War Information.

leucopenic states one is confronted with a variety of mechanism, bacterial toxin, therapeutic toxin, chemical and physical toxins, all of which are alike able to disturb the nucleic acid metbolism producing a closely related clinical picture. The author maintains that it is necessary to consider agranulocytosis by viewing the whole picture of leucopenia and the entire group of conditions manifesting depression of bone marrow function and in this connection we must group together: infections, intoxications and physiologic derangements involving the reticuloendothelial system and inducing among other signs as a depression of the white cell count. When this is done we enlarge our concept of mucous membrane lesions and their relation to nucleotide therapy. It has been found out that adenylic acid or substances containing it have both clinically and experimentally exercised a correctional influence on leucopenia.

SURGERY

Sterilization of Sulphanilamide Powder

The Medical Research Council recently called a conference which was attended by clinicians, bateriologists, and representatives of the Association of British Chemical Manufacturers, to consider methods of sterilization of sulphanilamide powder for local application.

For the *small-scale sterilization of sulphanilamide powder in hospitals*, etc., the following alternative procedures were recommended:

(A) Dry heat maintained at 150°C. for one hour in a paraffin bath, with the technique proposed by. H. Berry as follows: "Use dry sterile cotton-wool-plugged test-tubes (5 inches × ¾ inch or smaller diameter). Half fill them with the dry powdered substance using a powder funnel. Flame the upper portion of the tubes and replug with the sterile plugs. Immerse to within one inch of the tops of the tubes in a liquid paraffin oil bath and maintain at 150°c. for one hour. If the tubes are to bee stored the plugs should be covered with cellophane or paper.

(B) Dry heat maintained at 150°C. for one hour in an electric oven, with precautions to ensure even heating throughout.

(C) Autoclaving in a dressing sterilizer by the technique and with the precautions proposed by W. J. Buckland as follows: "An autoclave with vacuum drying attachment (dressing sterilizer) is used and the container is a dry boiling-tube plugged with non-absorbent wool. The boiling-tube must be thoroughly dried, if possible in a hot-air oven. (1) The jacket pressure of the sterilizer should be ready at a pressure of 20 to 30 lb. (2) Allow steam at 20 lb. into the empty closed chamber of the autoclave and leave for five minutes. (3) Using the appropriate valves clear chamber of all steam and condensed water. This process has heated the chamber, and the boiling-tubes, loosely plugged with non-absorbent wool and containing the powder (in 5- or 10-g. batches), are now placed in it. They should be placed on their sides, with the powder spread over their full length, giving a thinner mass for the steam to penetrate. (4) Leave the tubes for 15 minutes in the hot chamber; this heats tubes and contents sufficiently to prevent condensation inside and on the powder. (5) Autoclave at 15 lb. for half an hour. (6) Clear the chamber of steam and any condensed water quickly, and allow vacuum of 10 to 15 inches for 15 minutes. (7) Remove tubes from autoclave, place a tight sterile plug of non-absorbent wool on the top of the one already in, and cap tubes with a suitable paper—preferably cellophane. Caking does not occur. If apparent caking is observed, it is only present while the powder is still hot, and when cool a tap on the side of the tube is all this necessary to show the sterile preparation to be desired soft powder".

A proviso should be added with each of these recommendations that a sulphanilamide powder to be satisfactory for local application should not cake or be more than slightly discoloured with any of the techniques proposed.

The recommendations of the conference related only to sulphanilamide powder, as the sulphonamide preparation most frequently applied locally. It may be mentioned, however, that the paraffin bath technique described by Berry is recommended by the author as being suitable also for the sterilization of sulphathiazole powder in hospital practice (*Brit. M. J.*, **1**:263, 1943).

Bacterial Contaminations in Sulphonamide Ointments*

Fisher and others (*J. A. M. A.*, **122**:855, 1943) writes that the rapidly growing use of sulphonamide powders, ointments and solutions for topical applications in wounds raises the question of the possibility of these substances becoming contaminated with pathogenic organisms against which these drugs are ineffective. In order to determine the self-sterilizing properties of ointments of sulphonamides alone and of ointments of the sulphonamides in combination with various oxidizing agents, a test was devised. Four gm. of the ointments was weighed into sterile glass jars, and 1 cc. of a 20-hour broth culture of the desired test organism was throughly mixed with the ointment. Subcultures consisting of a 4mm. loopful of the ointment-organism mixture into nutrient or defibrinated blood broth mediums were taken at specified time intervals. In all instances, presence or absence of growth was checked after 24 hours incubation at 37°C. of the orginal subcultures, by smear, or by planting on nutrient or blood agar plates. It was concluded that 5 per cent sulphanilamide, sulphathiazole or sulphadiazine ointments in a water dispersible base may become contaminated with disease producing organisms which these drugs are not capable of killing (Clostridium welchi, staphylococci, etc.). The addition of small amounts of other chemicals, particularly certain oxidising agents, increases the self-sterilizing properties of these ointments. The most practical and generally effective agent examined appears to be urea peroxide in up to 1 per cent concentration. Higher concentrations, however, increase the irritant properties and make the substances objectionable for certain uses. The authors emphasize that these results indicate the need for careful manufacture of sulphonamide products intended for topical application. The addition of an antiseptic to enhance the bactericidal properties and insure sterility of sulphonamide ointments is, they say, essential as a factor of safety.

* Abstract through courtesy of the United States Office of War Information.

PHARMACOLOGY

Toxic Reactions to Succinyl Sulphathiazole

Clay and Pickwell (*J.A.M.A.*, **123**:203, 1943) write to say that succinyl sulphathiazole is advertised as a clinically non-toxic intestinal bacteriostat. Admittedly, unfavourable reactions are uncommon—much more so than with sulphanilyl guanidine, but toxic phenomena do occur.

Poth mentions infrequent complaints in headache, dizziness and anorexia. He cites a single case in which 0·25 Gm. (presumably per kilogram) of the drug had been administered daily for eight days for chronic ulcerative colitis with complaints of headache, nausea, vomiting, chills and arthralgia associated with a temperature of 103°F., lesions similar to erythema nodosum on the anterior surfaces of the legs, moist rales in the chest and a 5 per cent eosinophilia. A week later, when the reaction had subsided, administration of a single gram of sulphathiazole produced a temperature of 103·6°F. and the symptoms and signs described in the first reaction. Smyth and his associates observed sulphonamide crystals in the urine of 10 to 14 patients treated with succinyl-sulphathiazole for Flexner dysentery but none in the urine of 10 patients hosiptalized for other causes and given succinyl-sulfathiazole as controls.

In a series of 100 hospitalized adult patients in Johns Hopkins Hospital receiving the drug for many diverse conditions in doses of 0·25 G/Kg. as an initial dose and as a daily dose divided into six equal portions there were only two unfavourable reactions, aside from a case of conjunctivitis, questionably due to the drug: first, a case of fever, rash and arthralgia similar to Poth's case, and the second, a case of crystalluria with hæmaturia. Brief case reports are presented with the following comments:—

Case I represents an instance of drug fever which, while not the first reported attributable to succinyl-sulphathiazole, is unusual in that it occurred so soon after initiation of therapy. It also indicates that as with other sulphonamides, arthralgia and rash may appear during the course of succinyl-sulphathiazole therapy. The second case is, so far as can be ascertained, the first one of hæmaturia attributable to this drug although crystalluria, which accompanied the hæmaturia, has previously been observed.

The authors make a plea for careful watching of the patients, frequent urine analysis and blood examination.

The Effect of Potassium and of the Cardiac Glucosides on the Vagus Reactions of the Heart and Stomach of the Turtle

Fetter and others (*Am. J. Dig. Dis.*, **10**:303, 1943) write that a great deal of experimental work on the action of potassium on the physiological structures of various types of animals has been done in recent years. Among other effects, Zwemer and Lowenstein have pointed out that in normal animals (mammals) the cardiac glucosides appear to protect against potassium poisoning, presumably by preventing a rise of plasma potassium. The object of the authors' experiments was to extend the knowledges of the effects of potassium and a cardiac glucoside upon the simultaneous activities of two mechanism under the control of autonomic system, namely, the heart and the gastrointestinal tract, where the vagus exerts opposite effects.

Potassium chloride alone, and strophosid alone, inhibits the response of the stomach to stimulation of vagus. The action of strophosid following the administration of potassium chloride brings about a return of the response of the stomach to vagal excitation in 9 cases. In 6 there was no effect. It may be that the two drugs unite to form a third product which increases the response of the stomach to the vagus unless the potassium chloride has had too detrimental an effect. On the contrary, the potassium chloride and strophosid separately lower the threshold for vagal inhibition of the heart. The response of the heart after strophosid and potassium chloride together is not much altered. Since these drugs have opposite effects upon the two organs to vagal excitation, the effects of the drugs cannot be on the nerve, but must take place in some structures beyond the nerve, *i.e.* on the myoneural junction or the muscle.

In conclusion, the authors say that the data obtained appear to indicate that in turtle hearts rendered more excitable by excess of potassium to vagal inhibition, the irritability is unaffected by subsequent administration of strophosid, while in stomachs rendered less irritable to excitation by potassium chloride the subsequent administration of the cardiac glucoside lowers the threshold for excitation by the vagus. This effect on the stomach seems to agree with Zwemen and Lowenstein work where they found that cardiac glucosides prevented the typical effects of potassium poisoning.

The Ergot Alkaloids and Involution of the Uterus

Equal in speed and efficiency to extracts of posterior pituitary for the control of postpartum atony and hæmorrhage, ergometrine possesses advantages over such extracts in that it is non-toxic and has no effect on the vascular or autonomic nervous system. These advantages are not yet appreciated by all who practise obstetrics, and cases of "pituitrin shock" mistaken for "obstetric shock' still occur.

The scientific basis of the traditional ergot therapy in the puerperium is certainly open to question. The process of involution is said to represent the most rapid type of atrophy known to occur in any tissue under either physiological or pathological conditions. If this is due to ischæmia brought about by the contraction and retraction of the uterine muscle fibres, then ergot should assist involution. But if the hypertrophy of the uterus during pregnancy is the result of the presence of large amounts of œstrogen in circulation and the mechanical stimulus of the products of conception, then it is reasonable to assume that the puerperal atrophy is the result of withdrawal of such factors. In such a case ergot, by increasing the rate and amplitude of contractions to the extent of inducing spasm, could not assist involution, but might well have an adverse effect by hindering the absorption of the products of autolysis.

In a recent paper Chassar Moir and Russel discuss the use of ergometrine and ergotamine during the puerperium. In a large series of cases the rate of involution was assessed by careful observation of the height of the fundus and of the amount and character of the lochia. Their findings, in contrast with the results of similar if less carefully controlled investigation by other workers, go to show that neither of these ergot alkaloids is beneficial to the process of involution.

Ergot alkaloids are often advised in the treatment of uterine puerperal infection, but, again, Chassar Moir and Russel record no decrease in the morbidity rate in patients given ergometrine and ergotamine. They argue, moreover, that as infection elsewhere in the body is treated by resting the infected tissue, it is unreasonable to induce activity in a uterus that it is infected. There is, however, a place for ergometrine in the treatment of those cases, not necessarily infected, in which the lochial discharge is partly retained in the uterus. In these days, when the supply of ergot and its alkaloids is limited and should be conserved, those clinicians who still prescribe them as a routine in the puerperium would do well to reconsider whether they should continue a practice which, if not harmful, is of doubtful value and is certainly wasteful.—Annotation, *Brit. M. J.*, **1**:270, 1943.

Status of Sulphonamide Therapy in Malaria

Johnson (*J. Am. Med. Sci.*, **205**:327, 1943) discusses the need for a new and effective antiperiodic, along with the present obstacles in the use of quinine derivatives. After describing the author's independent work on the antimalarial action of sulphadiazine, and of sulphathiazole as a point of premedication he gives a resume of the work of Schwartz *et al.* which indicates that sulphathiazole in their hands was effective as an antimalarial in only 50 per cent of the cases. The work of Cogeshall *et al.* with the sulphonamides, promin and sulphadiazine, in the treatment of naturally acquired and therapeutic malaria has also been reviewed. Results in the latter was inconclusive but were indicative that the sulphonamides possessed an antimalarial action in both naturally acquired and therapeutic malaria. Sulphanilamide was found to be without effect in human malaria.

The author studied the effects of sulphadiazine on asexual artificially induced malaria where the patients under study could be kept under observation for a comparatively long time which would aid materially in determining the rate of relapse after treatment. To that end he employed a strain of quartan which has been in constant use for a period of more than 10 years and has long since become asexualised; and produces a very regular quartan fever pattern where spontaneous remissions rarely occur. All patients were kept at rest but were allowed bathroom priviledges. Usually no other medicine was given. The usual routine in the clinic of giving 4 intravenous injections of mapharsen was abandoned on account of the antiperiodic effect of this trivalent arsenical. This was done to enhance the evaluation of the sulphonamide therapy. A number of different treatment schedules were used in the several cases treated. The general principle of heavier dose on the first day or two followed by a reduced maintenance dosage was adhered to in all cases. The two accompanying tables give the relevent details. The author gives the following conclusions: 1. Sulphadiazine is an effective anti-malarial. 2. It is exhibited with a minimum of toxic reaction and is, therefore, taken by patients with less reluctance than quinine. 3. The relapse rate, employing the dosage schedules and in therapeutic quartan malaria, has been established at 23%. The amount of treatment used appeared to have no relation to the relapse rate. Patients suffering from relapses had had 5, 8, and 9 days of treatment respectively. 4. Relapses are controlled by a second course of sulphadiazine. No patient has had a second relapse. 5. The antimalarial action of sulphadiazine could be used to advantage by the military in malarious areas.

Case No.	*Type Malaria used*	*Drug used*	*Days treatment*	*Amount in gm.*	*Pre-treatment smears*	*Smears after treatment*	*Days since treatment*	*Relapse*	*Toxic reaction*
13165	Q	Diazine	7	36	Pos.	Neg.	239	No	No
13148	Q	Diazine	8	40	Pos.	Neg.	248	Yes	No
13194	Q	Diazine	7	36	Pos.	Neg.	227	No	No
12503	Q	Diazine	5	28	Pos.	Neg.	198	No	No
13190	Q	Diazine	8	28	Pos.	Neg.	264	No	No
13206	T	Diazine	5	28	Pos.	Neg.	204	Yes	Yes
12882	Q	Diazine	4	24	Pos.	Neg.	190	No	No
12501	Q	Diazine	4	24	Pos.	Neg.	179	No	No
13247	Q	Diazine	4	24	Pos.	Neg.	186	No	No

Patients in this series received from 4 to 8 days of sulphonamide treatment while those in series No. 2 received either 9 or 10 days of treatment each. It was intended to run the series in order to compare efficiency of shorter and longer courses but small number of cases in series No. 2 would not permit statistical comparison of any value. Relapse rates are computed on basis of total number of patients in the two series.

T=Tertian. Q=Quartan.

Case No.	*Type Malaria used*	*Drug used*	*Days treatment*	*Amount in gm.*	*Pre-treatment smears*	*Smearrs after treatment*	*Days since treatment*	*Relapse*	*Toxic reaction*
13300	Q	Diazine	10	48	Pos.	Neg.	124	No	No
13297	Q	Diazine	9	44	Pos.	Neg.	116	Yes	Yes
13323	Q	Diazine	10	46	Pos.	Neg.	73	No	No
13345	Q	Diazine	10	46	Pos.	Neg.	70	No	No

This series consisted of 4 patients. Treatment periods were 9 to 10 days and the total dosage of sulphadiazine was from 44 to 48 gm. There was one relapse in the 4 cases.

T=Tertian. Q=Quartan.

BOOK REVIEWS

PATHOLOGICAL HISTOLOGY—By ROBERTSON F. OGILVIE. Second Edition, 1943. Pages xii+411. Demy 8 vo.. With 235 photomicrographs in colour. Published by E. & S. Livingstone, Edinburgh. Price 32 s.

Morbid anatomy and histology form the stepping-stone to medical science and only a comprehensive knowledge of the same will enable the medical student to grasp the causation and significance of symptoms and signs. Evidently, much depends on how an undergraduate learns the basic subject, *i.e.*, pathology. Standard books on the subject are many, and teaching in the class is expected to be as it should be. But even then the student experiences difficulties when he wants to revise his morbid histological slides and recapitulate the salient features. He is likely to find that he has forgotten what particular features he is to look for in a particular slide. Similar is the difficulty to the graduate who has a chance to return to morbid histology.

The present volume has been intended to solve these difficulties in both undergraduates and graduates. The outstanding feature is the introduction of representative colour-photographs of the histological appearances of tissues resulting from disease. We must appreciate the skill of Mr. T. C. Dodds in interpreting the Finlay process of colour-photography and helping in the production of a book, unique of its kind. The inclusion of brief eitological discussion and macroscopic appearance has further enhanced the worth of the book.

No adverse criticism is really possible though, a brief consideration of the histology of the common tropical splenomegalies, such as malaria and kala-azar, would have made the book more comprehensive specially for the students in the tropics.

Anyway the book rightly serves the purpose of what the author says in his preface, *viz.*, "a companion to a standard text-book of pathology and to meet the need of the student in the class of morbid histology and of the graduate seeking more specialised knowledge in pathological processes" and every student of pathology will find this book to be an excellent addition.

B. P. TRIBEDI.

HYGIENE FOR NURSES—By JOHN GREY, and G. J. I. LINKLATER. Sixth Edition, 1943. Pages viii+240. Crown 8 vo. Published by E. & S. Livingstone, Edinburgh. Price 5s.

This standard text book of hygiene for nurses has already made its position which it deserves. The book has been modelled on the syllabus issued by the General Nursing Council. The special point of the book is that it has been written with the idea of not only preparing the candidates to pass the test on hygiene but to prepare them for this professional life. In professional life, personal hygiene is essential for the success of a good nurse and naturally the book has laid great stress on these points without sacrificing any essential feature. In 13 well-written chapters the authors have discussed personal hygiene, food and metabolism, vegetable foods and animal foods, internal parasites, external parasites, communicable diseases, the house, air and ventilation, lighting, heating, water, sewage disposal, and, the nurse in her relation to public health, which is the last chapter gives the broader outlook of the nursing problem. The authors have opined, "Public health authorities, having dealt with his environment, are now more concerned with the preservation of the health of the individual. In order to do so, the attempt is being made, and not unsuccessfully, to convey the knowledge and practice of hygiene to each separate citizen, for it is realised that it is only the aggregate of healthy individuals which makes for good public health." In the appendices, a scheme of the department of health, a list of notifiable diseases, incubation and quarantine periods and composition of various foods have been dealt with. Inclusion of question papers will be much appreciated by probationer nurses.

I.M.A. AND DRUG CONTROL ORDER, 1943

The following is the extract of a letter received by the Central Office, I.M.A. from the Department of Industries and Civil Supplies of the Government of India:

" * * * medical practitioners are, under the Drugs Control Order, 1943, required to take out retailer's licences in Form 'A' if they sell any of the drugs specified in parts (i) and (ii) of schedule 'A' in unopened containers to the public or to their own patients. They are not required to take out retailer's licences if they supply dispensed medicines to their patients or if they supply as a part of their treatment to their own patients loose tablets, etc. of proprietary medicines normally kept in stock by bonafide doctors or if they personally and directly, administer injections, ointments, etc., specified in parts (i) and (ii) of the schedule or supply in an emergency drugs mentioned in parts (i) and (ii) of the schedule which are normally kept by docotrs for use in emergencies. Thus if a doctor sells a complete unopened bottle of Blaud Pills to his patients he must have a licence. If he merely supplies them a mixture of drugs specified in part (iii) of the schedule or gives them an injection of Emetine or applies Tannafax ointment or in an emergency supplies mepacrine tablets he does not need a licence.

"Under the Drugs Control Order, 1943, medical practitioners are required to take out purchasers' licences in Form 'B' for the purchase of controlled drugs from manufacturers, importers and wholesalers."